U Urology

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Acronyms

β-hCG	beta-human chorionic gonadotropin
ABx	antibiotics
AFP	alpha-fetoprotein
ART	assisted reproductive technologies
AUA	American Urology Association
BCG	Bacillus Calmette-Guérin
BPH	benign prostatic hyperplasia
CAH	congenital adrenal hyperplasia
CaP	prostatic carcinoma
CBI	continuous bladder irrigation
CFU	colony-forming unit
CHF	congestive heart failure
CIC	clean intermittent catheterization
CIS	carcinoma *in situ*
CMG	cystometrogram
CPPS	chronic pelvic pain syndrome
CTU	CT urography
CUA	Canadian Urological Association
CVA	costovertebral angle
d/c	discharge
DHT	dihydrotestosterone
DMSA	dimercaptosuccinic acid
DRE	digital rectal exam
DSD	detrusor sphincter dyssynergia
EBRT	external beam radiation therapy
ED	erectile dysfunction
EPS	expressed prostatic secretions
ESWL	extracorporeal shockwave lithotripsy
FNA	fine needle aspiration
GA	general anesthesia
GAG	glycosaminoglycan
HIFU	high-intensity focused ultrasound
HPF	high power field
HPTA	hypothalamic-pituitary-testicular axis
ICSI	intracytoplasmic sperm injection
IFN-α	interferon-alpha
IL-2	interleukin-2
IPSS	International Prostate Symptom Score
ISD	intrinsic sphincter deficiency
IUI	intrauterine insemination
IVF	*in vitro* fertilization
IVP	intravenous pyelogram
KUB	kidneys, ureters, bladder
LFT	liver function test
LMN	lower motor neuron
LUTS	lower urinary tract symptoms
MAG3	mercaptoacetyltriglycine
MET	medical expulsive therapy
MS	multiple sclerosis
NSGCT	non-seminomatous germ cell tumour
PCKD	polycystic kidney disease
PCNL	percutaneous nephrolithotomy
PDE	phosphodiesterase
PID	pelvic inflammatory disease
PMC	pontine micturition centre
POD	post-obstructive diuresis
PSA	prostate specific antigen
PUV	posterior urethral valve
PVD	peripheral vascular disease
PVR	post-void residual
QOL	quality of life
RCC	renal cell carcinoma
RFA	radio-frequency ablation
RP	radical prostatectomy
RPLND	retroperitoneal lymph node dissection
RTA	renal tubular acidosis
RUG	retrograde urethrogram
SA	semen analysis
SCC	squamous cell carcinoma
SUI	stress urinary incontinence
TMP/SMX	trimethoprim/sulfamethoxazole
TRUS	transrectal ultrasound
TUIP	transurethral incision of the prostate
TUNA	transurethral needle ablation
TURBT	transurethral resection of bladder tumour
TURP	transurethral resection of the prostate
U/A	urinalysis
U/O	urine output
U/S	ultrasound
UCC	urothelial carcinoma
UMN	upper motor neuron
UPJ	ureteropelvic junction
URS	ureteroscopy
UTI	urinary tract infection
UVJ	ureterovesicular junction
VB1	voided bladder, initial (urethra)
VB2	voided bladder, midstream (bladder)
VB3	voided bladder, post-massage/digital rectal exam
VCUG	voiding cystourethrogram
VIU	visual internal urethrotomy
VUR	vesicoureteral reflux

Basic Anatomy Review

- recall that the anatomical position of the penis is erect; therefore, the anatomical ventral side of the penis appears to be the dorsal side of the flaccid penis

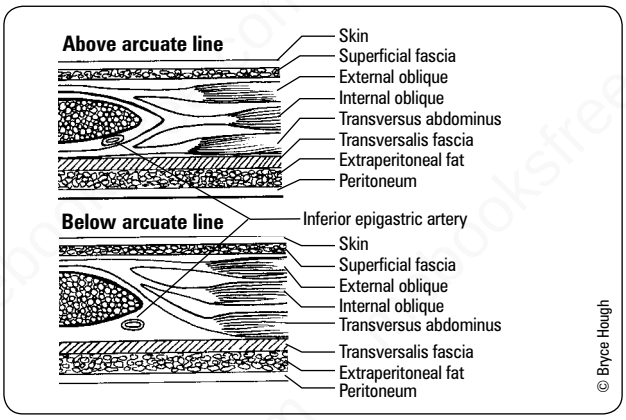


Figure 1. Midline cross-section of abdominal wall

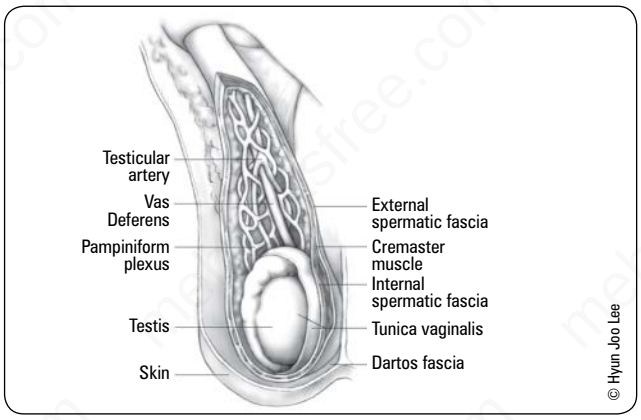


Figure 2. Anatomy of scrotum

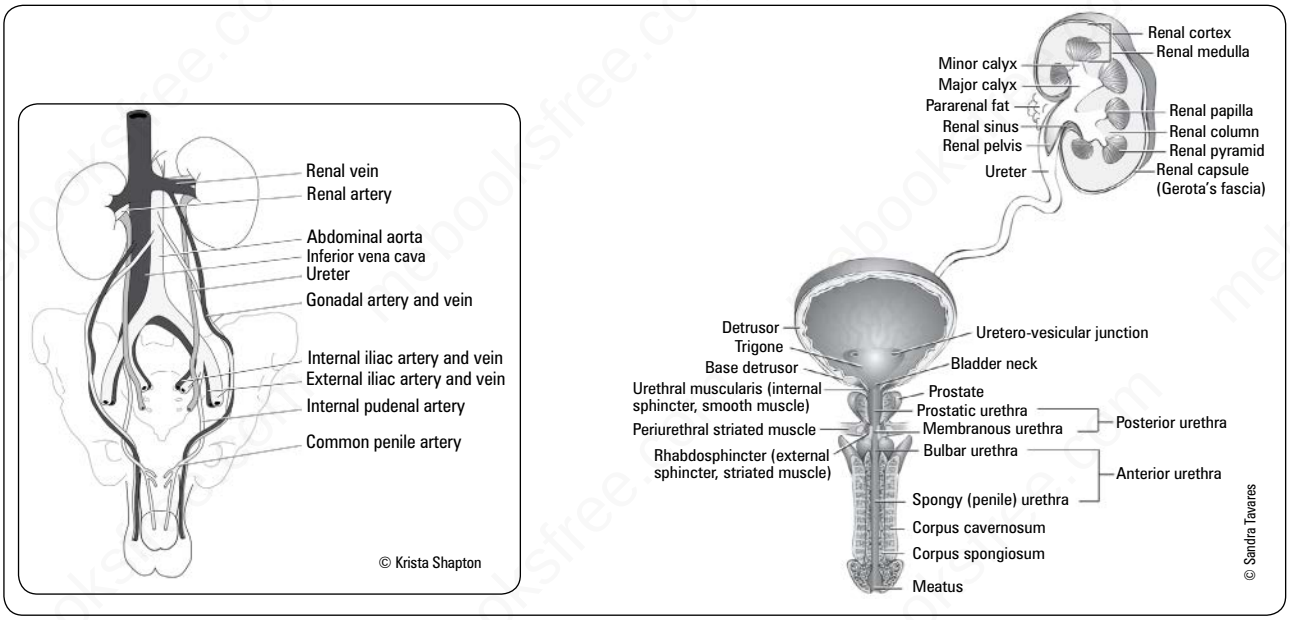


Figure 3. Essential male genitourinary tract anatomy

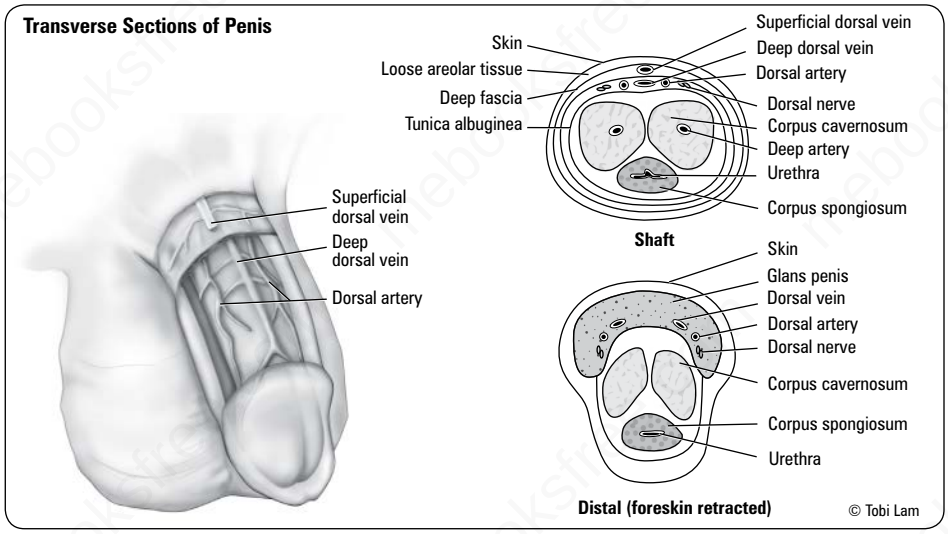


Figure 4. Cross section of the penis

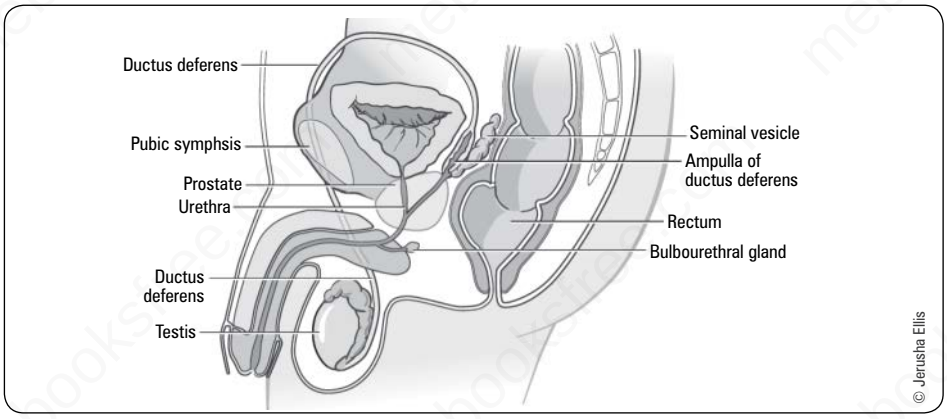


Figure 5. Median sagittal section of the male pelvis and perineum

Urologic History

- follow OPQRSTUVW approach
  - note that pain may not be limited to the genital region (e.g. lower abdomen, CVA)
- inquire about risk factors: past urologic disease (e.g. UTI, stones, STI, cancers, anatomic abnormalities), family Hx, medications, lifestyle factors (smoking, alcohol, inactivity), trauma, previous surgical procedures
- urinary habits
  - frequency of voiding, incontinence, nocturia
  - specific urinary symptoms include
    - storage symptoms: frequency, nocturia, incontinence, urgency (rush to toilet), stress (leak with cough/laughter)
    - voiding symptoms: straining, hesitancy, dysuria, intermittency, post-void dribbling, reduced stream, feeling of incomplete voiding
  - hematuria: blood clots, red/pink tinged urine
- sexual function
  - scrotal mass: see *Scrotal Mass*, U29
  - ED: see *Erectile Dysfunction*, U30
  - infertility: see *Infertility*, U34
- associated symptoms
  - N/V
  - bowel dysfunction
- constitutional symptoms
  - fever, chills, unintentional weight loss, night sweats, fatigue, malaise, bone pain

Always ask about sexual function on history. Change in erectile function can be one of the first symptoms that there is concomitant vascular disease. If there is new onset ED, consider screening for DM and CAD risk factors

Hematuria (Blood in the Urine)

Macroscopic (Gross) Hematuria

Definition
- blood in the urine that can be seen with the naked eye

Classification
- see Nephrology, NP21

Etiology

Table 1. Etiology by Age Group

Age (yr)	Etiology	
0-20	UTI, glomerulonephritis, congenital abnormalities	
20-40	UTI, stones, bladder tumour, exercise	
40-60	Male: bladder tumour, stones, UTI	Female: UTI, stones, bladder tumour
>60	Male: BPH, bladder tumour, UTI, RCC	Female: bladder tumour, UTI, RCC

Table 2. Etiology by Type

Pseudohematuria	Infectious/ Inflammatory	Malignancy	Benign	Structural	Hematologic
Vaginal bleeding Dyes (beets, rhodamine B in candy and juices) Hemoglobin (hemolytic anemia) Myoglobin (rhabdomyolysis) Drugs (rifampin, phenazopyridine, phenytoin) Porphyria Laxatives (phenolphthalein)	Pyelonephritis Cystitis Urethritis Glomerulonephritis Interstitial nephritis Tuberculosis	RCC (mainly adults) UCC Wilms' tumour (mainly pediatric) Leukemia	BPH Polyps Exercise-induced	Stones Trauma Foreign body Urethral stricture Polycystic kidneys Arteriovenous malformation Infarct Hydronephrosis Fistula	Anticoagulants Coagulation defects Sickle cell disease Thromboembolism

History
- timing of hematuria in urinary stream
  - initial: anterior urethra
  - terminal: bladder neck and prostatic urethra
  - total: bladder and/or above
- associated symptoms (storage and voiding)
  - pyuria, dysuria: UTI
  - flank pain, radiation: ureteral obstruction
- recent URTI: post-infectious glomerulonephritis, IgA nephropathy

Investigations
- CBC (rule out anemia, leukocytosis), electrolytes, Cr, BUN, INR, PTT
- urine studies
  - U/A, C&S, cytology
- imaging
  - CT contrast has largely replaced IVP to investigate upper tracts
  - consider contraindications: allergy, renal insufficiency, pregnancy
  - U/S alone may not be sufficient
  - cystoscopy to investigate lower tract (possible retrograde pyelogram)

Acute Management of Severe Bladder Hemorrhage
- manual irrigation via catheter with normal saline to remove clots
- Continuous Bladder Irrigation (CBI) using large (22-26 Fr) 3-way Foley to help prevent clot formation
- cystoscopy if active bleeding
  - identify resectable tumours
  - coagulate obvious sites of bleeding
- refractory bleeding
  - bilateral nephrostomy tube placement
  - hyperbaric oxygen
  - intravesical agents
    - continuous intravesical irrigation with 1% aluminum potassium sulfate solution as needed
    - intravesical instillation of 1% silver nitrate solution
    - intravesical instillation of 1-4% formalin (requires GA and pre-procedure cystogram to rule out reflux)
  - embolization or ligation of iliac branches
  - cystectomy and diversion (rarely performed)

Gross, painless hematuria in adults is bladder cancer until proven otherwise

Common Urologic Causes of Hematuria can be Classified as:

TICS
Trauma/**T**umour/**T**oxins
Infection/**I**nflammatory
Calculi/**C**ysts
Surgery/**S**ickle cell and other hematological causes

Upper Tract Imaging Options
CT Urography (CTU): test of choice for renal parenchyma, calculi, and infections. Involves exposure to radiation and IV contrast (assess renal function and allergies)
U/S: Superior to IVP for evaluation of renal parenchyma and renal cysts; limited sensitivity for UCC and small renal masses; U/S alone is insufficient for upper tract imaging
Intravenous Pyelogram (IVP): Traditional option but rarely used (replaced by CTU); reasonable sensitivity for UCC, but poor sensitivity for RCC

Microscopic Hematuria

Definition
- blood in the urine that is not visible to the naked eye
- ≥2 RBCs/HPF on urinalysis of at least two separate samples

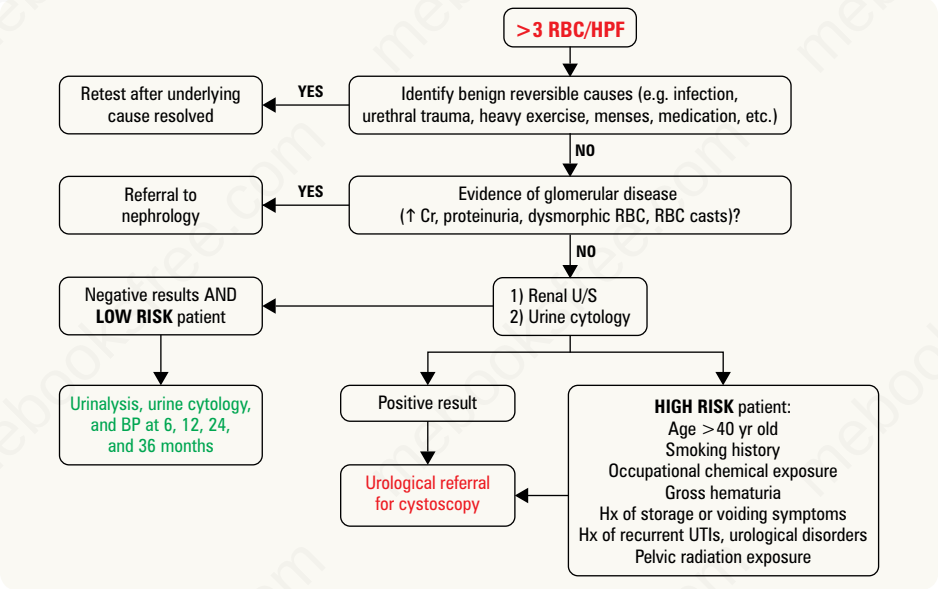

>3 RBC/HPF
Identify benign reversible causes (e.g. infection, urethral trauma, heavy exercise, menses, medication, etc.)
YES
Retest after underlying cause resolved
NO
Evidence of glomerular disease (↑ Cr, proteinuria, dysmorphic RBC, RBC casts)?
YES
Referral to nephrology
NO
1) Renal U/S
2) Urine cytology
Negative results AND LOW RISK patient
Urinalysis, urine cytology, and BP at 6, 12, 24, and 36 months
Positive result
Urological referral for cystoscopy
HIGH RISK patient:
Age >40 yr old
Smoking history
Occupational chemical exposure
Gross hematuria
Hx of storage or voiding symptoms
Hx of recurrent UTIs, urological disorders
Pelvic radiation exposure

Figure 6. Workup of asymptomatic microscopic hematuria
Based on CUA Guidelines. Alternatively, the AUA recommends cystoscopy and CT urogram for all patients with confirmed microscopic hematuria; follow-up for negative workup is urinalysis yearly for two years, with repeat anatomic evaluation if microscopic hematuria persists

Lower Urinary Tract Dysfunction

- see Gynecology for relevant female topics
- the lower urinary tract consists of the bladder and urethra. LUTD frequently involves both parts

Voiding

- two phases of lower urinary tract function
  1. storage phase (bladder filling and urine storage)
     - accommodation and compliance
     - no involuntary contraction(s)
  2. voiding phase (bladder emptying)
     - coordinated detrusor contraction
     - synchronous relaxation of outlet sphincters
     - no anatomic obstruction
- voiding dysfunction can therefore be classified as
  - failure to store: due to bladder or outlet
  - failure to void: due to bladder or outlet
- three types of symptoms
  - storage (formerly known as irritative)
  - voiding (formerly known as obstructive)
  - post-voiding

Urinary Incontinence

Definition
- involuntary leakage of urine

Etiology
- urgency incontinence
  - detrusor overactivity
    - CNS lesion, inflammation/infection (cystitis, stone, tumour), bladder neck obstruction (tumour, stone), BPH, idiopathic
  - decreased compliance of bladder wall (inability to store urine)
    - CNS lesion, fibrosis
    - sphincter/urethral problem

- stress urinary incontinence (SUI)
  - common in women; seen in men after prostate cancer treatment or pelvic operations
  - urethral hypermobility
    - weakened pelvic floor and musculofascial urethral and vaginal supporting mechanisms allows bladder neck and urethra to descend with increased intra-abdominal pressure
    - urethra is pulled open by greater motion of posterior wall of outlet relative to anterior wall
    - associated with childbirth, pelvic surgery, aging, levator muscle weakness, obesity
  - intrinsic sphincter deficiency (ISD): weakness of the urethra and associated smooth and striated muscle elements
  - pelvic surgery, neurologic problem, aging and hypoestrogen state
  - ISD and urethral hypermobility frequently co-exist
- mixed incontinence
  - combination of stress and urgency incontinence
- overflow incontinence
  - is a term sometimes used to describe urinary incontinence associated with urinary retention; for causes of urinary retention see Table 4
  - use of the term should be accompanied by the associated pathophysiology (e.g. BPH with overflow incontinence)

Epidemiology
- variable prevalence in women: 25-45%
- F:M = 2:1
- more frequent in the elderly, affecting 5-15% of those living in the community and 50% of nursing home residents

Table 3. Urinary Incontinence: Types and Treatments

Type	Urgency	Stress	Mixed
Definition	Involuntary leakage of urine preceded by a strong, sudden urge to void	Involuntary leakage of urine with sudden increases in intra-abdominal pressure	Urinary leakage associated with urgency and increased intra-abdominal pressure
Etiology	Bladder (detrusor overactivity)	Urethra/sphincter weakness, post-partum pelvic musculature weakness	Combination of bladder and sphincter issues
Diagnosis	Hx Urodynamics	Hx Urodynamics Stress test (valsalva/cough)	Hx Urodynamics Stress test
Therapy	Lifestyle changes (fluid alterations, diet, etc.) Bladder habit training Anticholinergics β-3-agonist Botulinum toxin A Neuromodulation	Weight loss Kegel exercises Bulking agents Surgery (slings, tension-free vaginal tape, retropubic urethropexy, artificial sphincter)	Combination of management of urgency and stress incontinence

Lower Urinary Tract Symptoms (LUTS)

Storage (FUND)
Frequency
Urgency
Nocturia
Dysuria

Voiding (SHED)
Stream changes
Hesitancy
Incomplete **E**mptying
Dribbling

Causes of Reversible Urinary Incontinence

DIAPERS
Delirium
Inflammation/Infection
Atrophic vaginitis/urethritis
Pharmaceuticals/**P**sychological
Excess U/O
Restricted mobility/**R**etention
Stool impaction

Urgency is the symptom of a strong need to void; it is not necessarily associated with incontinence

Lower Urinary Tract Symptoms (LUTS)

Urinary Retention

Table 4. Etiology of Urinary Retention

Outflow Obstruction	Bladder Innervation	Pharmacologic	Infection
Bladder neck or urethra: calculus, clot, foreign body, neoplasm, neurological (DSD) Prostate: BPH, prostate cancer Urethra: stricture, phimosis, traumatic disruption Miscellaneous: constipation, pelvic mass	Intracranial: CVA, tumour, Parkinson's, cerebral palsy Spinal cord: injury, disc herniation, MS DM Post-abdominal or pelvic surgery	Anticholinergics Narcotics Antihypertensives (ganglionic blockers, methyldopa) OTC cold medications containing ephedrine or pseudoephedrine Antihistamines Psychosomatic substances (e.g. ecstasy)	GU: UTI, prostatitis, abscess, genital herpes Infected foreign body Varicella zoster

Acute vs. Chronic Retention
Acute retention is a medical emergency characterized by suprapubic pain and anuria with normal bladder volume and architecture
Chronic retention can be painless with greatly increased bladder volume and detrusor hypertrophy followed by atony (late)

If a trauma patient is unable to void, has blood at urethral meatus, a scrotal hematoma, or a high riding prostate, there is urethral injury until proven otherwise so catheterization is CONTRAINDICATED unless performed by urology staff or resident

Clinical Features
- suprapubic pain (with acute retention), incomplete emptying, weak stream
- palpable and/or percussible bladder (suprapubic)
- possible purulent/bloody meatal discharge (with UTI)
- increased size of prostate or reduced anal sphincter tone on DRE
- neurological: presence of abnormal or absent deep tendon reflexes, reduced "anal wink", saddle anesthesia

Investigations
- CBC, electrolytes, Cr, BUN, U/A and urine C&S, U/S, cystoscopy, urodynamic studies, PVR

Patients with ascites may have a falsely elevated PVR measured by bladder scan

Treatment
- treat underlying cause
- catheterization
  - acute retention
    - immediate catheterization to relieve retention; leave Foley in to drain bladder; follow-up to determine cause; closely monitor fluid status and electrolytes (risk of POD)
  - chronic retention
    - intermittent catheterization by patient may be used; definitive treatment depends on etiology
- suprapubic catheter if obstruction precludes urethral catheter
- for post-operative patients with retention:
  - encourage ambulation
  - α-blockers to relax bladder neck outlet
  - may need catheterization
  - definitive treatment will depend on etiology

Benign Prostatic Hyperplasia

Definition
- periurethral hyperplasia of stroma and epithelium in prostatic transition zone
- prostatic smooth muscle cells play a role in addition to hyperplasia

Etiology
- unknown
  - DHT required (converted from testosterone by 5-α reductase)
  - possible role of impaired apoptosis, estrogens, other growth factors

Epidemiology
- age-related, extremely common (50% of 50 yr olds, 80% of 80 yr olds)
- 25% of men will require treatment

Clinical Features
- result from outlet obstruction and compensatory changes in detrusor function
- voiding and storage symptoms
- DRE
  - prostate is smooth, rubbery, and may be symmetrically enlarged
- complications
  - retention
  - overflow incontinence
  - hydronephrosis
  - renal insufficiency
  - infection
  - gross hematuria
  - bladder stones

Investigations
- Hx, assessing LUTS and impact on QOL
  - may include self-administered questionnaires (IPSS or AUA symptom index for severity, progression, and treatment response)
- P/E, including DRE
- U/A to exclude UTI
- Cr to assess renal function
- renal U/S to assess for hydronephrosis
- PSA to rule out malignancy (see *Prostate Cancer Screening*, U26)
- uroflowmetry to measure flow rate (optional)
- PVR (optional)
- consider cystoscopy or bladder ultrasound prior to potential surgical management to evaluate outlet and prostate volume
- biopsy if suspicious for malignancy, i.e. elevated PSA or abnormal DRE

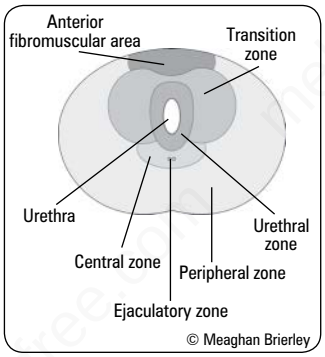


Figure 7. Cross-section of prostate

Prostate size does not correlate well with symptoms in BPH

Approximate Prostate Sizes
20 cc – chestnut
25 cc – plum
50 cc – lemon
75 cc – orange
100 cc – grapefruit

AUA BPH Symptom Score

FUNWISE
Frequency
Urgency
Nocturia
Weak stream
Intermittency
Straining
Emptying, incomplete feeling of

Each symptom graded out of 5
0-7: Mildly symptomatic
8-19: Moderately symptomatic
20-35: Severely symptomatic
Note: dysuria not included in score but is commonly associated with BPH

Initial alpha-adrenergic antagonist monotherapy for score <20, combination therapy for score >20

Treatment

Table 5. Treatment of BPH

	Conservative	Medical	Surgical	Minimally Invasive Surgical Therapies
When to use	Asymptomatic patients or symptomatic without bother	Moderate to severe symptoms that are distressing for patient	Significant symptom burden, acute urinary retention, refractory hematuria, recurrent infections	Patients who wish to avoid or may not tolerate surgery
Options	Watchful waiting: 50% of patients improve spontaneously	Lifestyle modifications (e.g. evening fluid restriction, planned voiding) α-adrenergic antagonists: reduce stromal smooth muscle tone 5-α reductase inhibitor: block conversion of testosterone to DHT; act to reduce prostate size Combination is synergistic Anti-cholinergic agents or β-3 agonist (for storage LUTS, without elevated PVR)	TURP (see U41) Laser ablation TUIP (prostate <30 g) Open prostatectomy	Microwave therapy TUNA Prostatic stent (not commonly used)

Men with planned cataract surgery should avoid starting α-adrenergic antagonists until after their surgery due to the risk of intraoperative floppy iris syndrome

BPH Surgery

Absolute Indication
Renal failure with obstructive uropathy
Refractory urinary retention

Relative Indications
Recurrent UTIs
Recurrent hematuria refractory to medical treatment
Renal insufficiency (rule out other causes)
Bladder stones

Urethral Stricture

Definition
- decrease in urethral calibre due to scar formation in urethra (may also involve corpus spongiosum)
- M>F

Etiology
- congenital
  - failure of normal canalization (i.e. posterior urethral valves)
- trauma
  - instrumentation/catheterization (most common)
  - external trauma (e.g. burns, straddle injury)
  - foreign body
- infection
  - long-term indwelling catheter
  - STI (gonococcal or chlamydial disease)
- inflammation
  - balanitis xerotica obliterans (BXO; lichen sclerosis or chronic progressive sclerosing dermatosis of the male genitalia) causing meatal and urethral stenosis

Clinical Features
- voiding and storage symptoms
- urinary retention
- hydronephrosis
- related infections: recurrent UTI, secondary prostatitis/epididymitis

Investigations
- laboratory findings
  - flow rates <10 mL/s (normal ~20 mL/s) on uroflowmetry
  - urine culture usually negative, but U/A may show pyuria
- radiologic findings
  - RUG and VCUG will demonstrate location
- cystoscopy

Treatment
- urethral dilatation
  - temporarily increases lumen size by breaking up scar tissue
  - healing will often reform scar tissue, recurrence of stricture
- visual internal urethrotomy (VIU)
  - endoscopically incise stricture
  - equal success rates to dilation with mid bulbar strictures <2 cm
  - high rate of recurrence (30-80%), avoid in younger patients
- open surgical reconstruction
  - complete stricture excision with anastomosis, ± urethroplasty depending on location and size of stricture

Combination therapy vs. alpha blocker or 5ARI
BJU Int 2011:107(6):946-54
Summary: Men with baseline prostate volume ≥40mL and baseline PSA ≥1.5 ng/mL had greater reductions in RR of BPH-related surgery and RR of clinical progression on combined therapy or dutasteride monotherapy than on tamulosin monotherapy.
Methods: 4-year combination of dutasteride and tamulosin study was a multicentre double-blind RCT of outcomes in men ≥50 years old with symptomatic BPH, with PSA ≥1.5ng/mL and ≤10ng/mL, and prostate volume ≤30mL. Patients received tamulosin, dutasteride or combination therapy. Primary endpoint was time to first acute urinary retention or BPH-related surgery; secondary endpoint was clinical progression of BPH/symptoms.
Results: Combination therapy resulted in significantly greater improvements in symptoms compared to dutasteride from 3 mo, and tamsulosin from 9 mo, and in BPH- related health status from 3 and 12 mo, respectively. There was a significant increase in ADE with combination therapy vs. monotherapies. However, withdrawal rates due to drug-related adverse events were similar across the treatment groups.

Finasteride for Benign Prostatic Hyperplasia
Cochrane DB Syst Rev 2010;10:CD006015
Purpose: To examine the effectiveness and safety of finasteride versus placebo or other active controls for the treatment of urinary tract symptoms.
Summary of Findings:
1. Finasteride improved urinary symptoms more than placebo in trails >1 yr duration and significantly lowered the risk of BPH progression.
2. Compared with α-blockers, finasteride was less effective than either doxazosin or terazosin, but equally as effective as tamsulosin.
3. Symptom improvement with finasteride + doxazosin is equal to doxazosin alone.
4. Finasteride treatment resulted in an increased risk of ejaculation disorder, impotence and lowered libido compared with placebo.
5. Compared with doxazosin and terazosin, finasteride had a lower risk of asthenia, dizziness, and postural hypotension.

Neurogenic Bladder

Definition
- dysfunction of the urinary bladder due to deficiency in some aspect of its innervation

Neurophysiology

Table 6. Efferent Sympathetic, Parasympathetic, and Somatic Nerve Supply

Nerve Fibres	Nerve Roots	Neurotransmitter/Receptor	Target
Sympathetic	T10-L2	NA/Adrenergic	Trigone, internal sphincter, proximal urethra (α receptors) Bladder body (β receptors))
Somatic (Pudendal)	S2-4	ACh/Nicotinic	External sphincter
Parasympathetic	S2-4	ACh/Muscarinic (M2, M3)	Detrusor

- stretch receptors in the bladder wall relay information to PMC and activate micturition reflex (normally inhibited by cortical input)
  - micturition
    - stimulation of parasympathetic neurons (bladder contraction)
    - inhibition of sympathetic and somatic neurons (internal and external sphincter relaxation, respectively)
  - urine storage
    - opposite of micturition
- voluntary action of external sphincter (pudendal nerve roots S2-S4) can inhibit urge to urinate
- cerebellum, basal ganglia, thalamus, and hypothalamus all have input at PMC in the brainstem

Microwave Thermotherapy for Benign Prostatic Hyperplasia
Cochrane DB Syst Rev 2012;9:CD004135
Purpose: To evaluate the efficacy and safety of microwave thermotherapy for the treatment of benign prostatic obstruction.
Selection Criteria: RCTs evaluating transurethral microwave therapy (TUMT) for men with symptomatic BPH with multiple comparison groups.
Results: 15 studies, 1,585 patients, mean age 66.8 yr, 3-60 mo duration. Mean urinary symptom scores decreased by 65% with TUMT and 77% with TURP. The pooled mean peak urinary flow increased by 70% with TUMT and 119% with TURP. Compared with TURP, TUMT was associated with decreased risks for retrograde ejaculation, treatment for strictures, hematuria, blood transfusions and transurethral resection syndrome, but increased risk for dysuria, urinary retention and retreatment for BPH symptoms.
Conclusions: Overall, microwave thermotherapy techniques are effective alternatives to TURP and α-blockers for treating symptomatic BPH, although less effective than TURP in improving symptom score and urinary flow.

Examples of Neurologic Voiding Dysfunction
- neurogenic detrusor overactivity (NDO)(formerly termed detrusor hyperreflexia)
  - lesion above PMC (e.g. stroke, tumour, MS, Parkinson's disease)
  - loss of voluntary inhibition of voiding
  - intact pathway inferior to PMC maintains coordination of bladder and sphincter
- detrusor sphincter dyssynergia (DSD)
  - suprasacral lesion of spinal cord (e.g. trauma, MS, arteriovenous malformation, transverse myelitis)
  - loss of coordination between detrusor and sphincter (detrusor contracts on closed sphincter and vice versa)
  - component of detrusor overactivity as well
- detrusor atony/areflexia
  - lesion of sacral cord or peripheral efferents (e.g. trauma, DM, disc herniation, MS, congenital spinal cord abnormality, post abdominoperineal resection)
  - flaccid bladder which fails to contract
  - may progress to poorly compliant bladder with high pressures
- peripheral autonomic neuropathy
  - deficient bladder sensation → increasing residual urine → decompensation (e.g. DM, neurosyphilis, herpes zoster)
- muscular lesion
  - can involve detrusor, smooth/striated sphincter

Nerve roots in micturition:
"S2-3-4 keeps the urine off the floor"

Neuro-Urologic Evaluation
- Hx and P/E (urologic and general neurologic)
- voiding diary
- catheterization volumes in patients with CIC
- U/A, renal profile
- imaging
  - U/S to rule out hydronephrosis and stones; occasionally CT scanning with or without contrast
- cystoscopy
- urodynamic studies
  - uroflowmetry to assess flow rate, pattern
  - filling CMG to assess capacity, compliance, detrusor overactivity
  - voiding CMG (pressure-flow study) to assess bladder contractility and extent of bladder outflow obstruction
  - video study to visualize bladder/bladder neck/urethra during CMG using x-ray contrast
  - EMG and video ascertains presence of coordinated or uncoordinated voiding, allows accurate diagnosis of DSD

"Spinal shock", initially manifests as atonic bladder

Treatment
- goals of treatment
  - prevent renal deterioration
  - prevent infections
  - achieve social continence

- clean intermittent catheterization (CIC)
- treatment options depend on status of bladder and urethra
  - bladder hyperactivity → anticholinergic medications to relax bladder (see *Urinary Incontinence*, U5)
    - if refractory
      - botulinum toxin injections into bladder wall
      - occasionally augmentation cystoplasty (enlarging bladder volume and improving compliance by grafting section of detubularized bowel onto the bladder)
      - occasionally urinary diversion (ileal conduit or continent diversion) in severe cases if bladder management unsuccessful
  - flaccid bladder → CIC

Dysuria

Definition
- painful urination

Etiology

Table 7. Differential Diagnosis of Dysuria

Infectious	Cystitis, urethritis, prostatitis, epididymitis/orchitis (if associated with lower tract inflammation), cervicitis, vulvovaginitis, perineal inflammation/infection, TB, vestibulitis
Neoplasm	Kidney, bladder, prostate, penis, vagina/vulva, BPH
Calculi	Bladder stone, urethral stone, ureteral stone
Inflammatory	Seronegative arthropathies (reactive arthritis: arthritis, uveitis, urethritis), drug side effects, autoimmune disorders, chronic pelvic pain syndrome (CPPS), interstitial cystitis
Hormonal	Endometriosis, hypoestrogenism
Trauma	Catheter insertion, post-coital cystitis (honeymoon cystitis)
Psychogenic	Somatization disorder, depression, stress/anxiety disorder
Other	Contact sensitivity, foreign body, radiation/chemical cystitis, diverticulum

Investigations
- focused Hx and P/E to determine cause (fever, d/c, conjunctivitis, CVA tenderness, back/joint pain)
  - any d/c (urethral, vaginal, cervical) should be sent for gonococcus/chlamydia testing; wet mount if vaginal d/c
  - U/A and urine C&S
  - if suspect infection, may start empiric ABx treatment (see Table 9, U12)
  - ± imaging of urinary tract (tumour, stones)

Hydronephrosis

- the upper urinary tract consists of the kidneys and ureters

Definition
- dilation of the renal pelvis and calyces caused by the impairment in antegrade urine flow

Etiology
- mechanical
  - congenital: see *Congenital Abnormalities*, U36
  - acquired
    - intrinsic: trauma, inflammation and bleeding, calculi, urologic neoplasms, BPH, urethral stricture, phimosis, previous urological surgery
    - extrinsic: trauma, neoplasms (uterine fibroid; colorectal, uterine, and cervical malignancies; lymphoma), aortic aneurysm, pregnancy (gravid uterus)
- functional
  - neuropathic: neurogenic bladder, diabetic neuropathy, spinal cord disease
  - pharmacologic: α-adrenergic agonists
  - hormonal: pregnancy (progesterone decreases ureteral tone)

Investigations
- focused Hx, inquiring about pain (flank, lower abdomen, testes, labia), U/O, medication use, pregnancy, trauma, fever, Hx of UTIs, calculi, PID, and urological surgery
- CBC, electrolytes, Cr, BUN, U/A, C&S
- imaging studies (U/S is >90% sensitive and specific)
  - MAG3 diuretic renogram: evaluates differential renal function and demonstrates if functional obstruction exists

Treatment
- hydronephrosis can be physiologic
- treatment should be guided at improving symptoms, treating infections, or improving renal function
- urgent treatment may require percutaneous nephrostomy tube or ureteral stenting to relieve pressure

Post-Obstructive Diuresis

Definition
- polyuria resulting from relief of severe chronic obstruction
- >3 L/24 h or >200 cc/h over each of two consecutive hours

Pathophysiology
- physiologic POD secondary to excretion of retained urea, Na^+, and H_2O (high osmotic load) after relief of obstruction
  - self-limiting; usually resolves in 48 h with PO fluids but may persist to pathologic POD
- pathologic POD is a Na^+-wasting nephropathy secondary to impaired concentrating ability of the renal tubules due to:
  - decreased reabsorption of NaCl in the thick ascending limb and urea in the collecting tubule
  - increased medullary blood flow (solute washout)
  - increased flow and solute concentration in the distal nephrons

Management
- admit patient and closely monitor hemodynamic status and electrolytes (Na^+ and K^+ q6-12h and replace prn; follow Cr and BUN to baseline)
- monitor U/O q2h and ensure total fluid intake <U/O by replacing every 1 mL U/O with 0.5 mL 1/2 NS IV (PO fluids if physiologic POD)
- avoid glucose-containing fluid replacement (iatrogenic diuresis)

Overactive Bladder

Definition
- a symptom complex that includes urinary urgency with or without urgency incontinence, urinary frequency (voiding ≥8 times in a 24 hr period), and nocturia (awakening ONE or more times at night to void)

Etiology
- multiple etiologies proposed
- symptoms usually associated with involuntary contractions of the detrusor muscle
- may be associated with other conditions such as SUI in women and BPH in men (see Table 8)
- may be neurogenic, myogenic or idiopathic

Epidemiology
- F:M= 1:1
- prevalence increases with age. 42% in males ≥75 years; 31% in females ≥75 years

Diagnosis
- the diagnostic process should document symptoms that define overactive bladder and exclude other disorders that could cause of the patient's symptoms
- minimal requirements for the process consist of:
  - focused history including past genitourinary disorders and conditions outlined in Table 8, questionnaires of LUTS for women and diaries of urination frequency, volume and pattern
  - P/E including genitourinary, pelvic and rectal examination
  - U/A to rule out hematuria and infection
- in some patients, the following investigations could be considered
  - post-void residual
  - cystoscopy to rule out recurrent infections, carcinoma in situ and other intravesical abnormalities
    - urodynamics to rule out obstruction in older men

Treatment
- non-pharmacological: behaviour therapies such as bladder training, bladder control strategies, pelvic floor muscle training, fluid management, and avoidance of caffeine, alcohol
- pharmacological
  - anti-muscarinics: oxybutynin hydrochloride, tolterodine, solifenacin, fesoterodine, or trospium
  - β3-adrenoceptor agonist: mirabegron
- refractory patients may be treated with:
  - neuromuscular-junction inhibition: botulinum toxin bladder injection
- others
  - percutaneous tibial nerve stimulation (not used commonly in Canada)
  - sacral neuromodulation

Table 8. Conditions that Could Contribute to Symptoms of Overactive Bladder

Lower Urinary Tract Conditions	UTI, obstruction, impaired bladder contractility
Neurological Conditions	Stroke, MS, dementia, diabetic neuropathy
Systemic Diseases	CHF, sleep disorders (primarily nocturia)
Functional and Behavioural	Excessive caffeine and alcohol, constipation, impaired mobility
Medication	Diuretics, anticholinergic agents, narcotics, calcium-channel blocker, cholinesterase inhibitors

Infectious and Inflammatory Diseases

Table 9. Antibiotic Treatment of Urological Infections

Condition	Drug	Duration
Urethritis	**Non-Gonococcal**	
	azithromycin (1 g PO)	x 1 d
	OR	
	doxycycline (100 mg PO bid)	7 d
	Gonococcal	
	ceftriaxone (250 mg IM) AND treat for *Chlamydia trachomatis*	x 1
Simple, Uncomplicated UTI	TMP-SMX (160 mg/800 mg PO bid)	3 d
	OR	
	nitrofurantoin (100 mg PO bid)	5 d
Complicated UTI	ciprofloxacin (1 g PO daily OR 400 mg IV q12h)	up to 2-3 wk
	OR	
	ampicillin (1 g IV q6h) + gentamicin (1 mg/kg IV q8h) (used for relatively short courses because of toxicity)	up to 2-3 wk
	OR	
	ceftriaxone (1-2 g IV q24h)	up to 2-3 wk
Recurrent/Chronic Cystitis	Prophylactic Treatment	
	Continuous: TMP-SMX (40 mg/200 mg PO qHS OR 3x/wk)	6-12 mo
	OR	
	nitrofurantoin (50-100 mg PO qHS)	6-12 mo
	Post-Coital: TMP-SMX (40 mg/200 mg-80 mg/400 mg)	within 2 h of coitus
	OR	
	nitrofurantoin (50-100 mg PO qd)	within 2 h of coitus
Acute Prostatitis	ciprofloxacin (500-750 mg PO bid)	2-4 wk
	OR	
	TMP-SMX (160 mg/800 mg PO bid)	4 wk
	OR	
	IV therapy with gentamicin and ampicillin, penicillin with β-lactamase inhibitor, 3rd gen cephalosporin, OR a fluoroquinolone	4 wk (IV and oral step-down)
Chronic Prostatitis	ciprofloxacin (500 mg PO bid)	4-6 wk
Epididymitis/Orchitis	<35 yr	
	ceftriaxone (200 mg IM)	x 1
	AND	
	doxycycline (100 mg PO bid)	10 d
	≥35 yr	
	ofloxacin (300 mg PO bid)	10 d
Acute Uncomplicated Pyelonephritis	ciprofloxacin (500 mg PO bid)	7 d
	± ceftriaxone (1 g IV) OR ciprofloxacin (400 mg IV)	x 1
	OR	
	IV therapy with a fluoroquinolone, gentamicin and ampicillin, extended spectrum cephalosporin, extended spectrum penicillin, OR a carbapenem	14 d total (IV and oral step-down)

Antibiotic therapy should always be based on local resistance patterns and adjusted according to culture and sensitivity results

Cystitis: Common Pathogens

KEEPS
K*lebsiella* sp.
E*. coli* (90%), other Gram-negatives
Enterococci
P*roteus mirabilis,* ***P****seudomonas*
S*. saprophyticus*

Acute uncomplicated pyelonephritis: suspected or confirmed *Enterococcus* infection requires treatment with ampicillin

Urinary Tract Infection

- for UTIs during pregnancy, see Obstetrics, OB28

Definition

- symptoms suggestive of UTI + evidence of pyuria and bacteriuria on U/A or urine C&S
  - if asymptomatic + 100,000 CFU/mL = asymptomatic bacteriuria; only requires treatment in certain patients (e.g. pregnancy)

Classification

- uncomplicated: lower UTI in a setting of functionally and structurally normal urinary tract
- complicated: structural and/or functional abnormality, male patients, immunocompromised, diabetic, iatrogenic complication, pregnancy, pyelonephritis, catheter-associated
- recurrent: see *Recurrent/Chronic Cystitis*

Risk Factors
- stasis and obstruction
  - residual urine due to impaired urine flow e.g. PUVs, reflux, medication, BPH, urethral stricture, cystocele, neurogenic bladder
- foreign body
  - introduce pathogen or act as nidus of infection e.g. catheter, instrumentation
- decreased resistance to organisms
  - DM, malignancy, immunosuppression, spermicide use, estrogen depletion, antimicrobial use
- other factors
  - trauma, anatomic abnormalities, female, sexual activity, menopause, fecal incontinence

Clinical Features
- storage symptoms: frequency, urgency, dysuria
- voiding symptoms: hesitancy, post-void dribbling, dysuria
- other: suprapubic pain, hematuria, foul-smelling urine
- pyelonephritis – if present: typically presents with more severe symptoms (e.g. fever/chills, CVA tenderness, flank pain)

Organisms
- typical organisms: KEEPS (*E. coli* 75-95%)
- atypical organisms
  - tuberculosis (TB)
  - *Chlamydia trachomatis*
  - *Mycoplasma* (*Ureaplasma urealyticum*)
  - fungi (*Candida*)

Prevention of UTIs
- Maintain good hydration (try cranberry juice)
- Wipe from front to back to avoid contamination of the urethra with feces from the rectum
- Avoid feminine hygiene sprays and scented douches
- Empty bladder immediately before and after intercourse

Indications for Investigations
- pyelonephritis
- persistence of pyuria/symptoms following adequate antibiotic therapy
- severe infection with an increase in Cr
- recurrent/persistent infections
- atypical pathogens (urea splitting organisms)
- Hx of structural abnormalities/decreased flow

Investigations
- U/A, urine C&S
  - UA: leukocytes ± nitrites ± hematuria
  - C&S: midstream, catheterized, or suprapubic aspirate
- if hematuria present, retest post-treatment, if persistent need hematuria workup (see *Microscopic Hematuria*, U5)
- U/S, CT scan if recurrent or treatment-resistant UTIs, suspected anatomic abnormalities, history indicates complicated cystitis

Treatment
- see Table 9, U12, *Antibiotic Treatment of Urological Infections*
- if febrile, consider admission with IV therapy and rule out obstruction

Recurrent/Chronic Cystitis

Definition
- ≥3 UTIs/yr

Etiology
- bacterial reinfection (80%) vs. bacterial persistence (relapse)
  - bacterial reinfection
    - recurrence of infection with either 1) a different organism, 2) the same organism if cultured >2 wk following therapy, or 3) with any organism with an intermittent sterile culture
  - bacterial persistence
    - same organism cultured within 2 wk of sensitivity-based therapy

Investigations
- assess predisposing factors
- investigations may include cystoscopy, U/S, CT

Treatment
- lifestyle changes (limit caffeine intake, increase fluid/H_2O intake)
- ABx: continuous vs. post-coital
- post-menopausal women: consider topical or systemic estrogen therapy
- no treatment for asymptomatic bacteriuria except in pregnant women or patients undergoing urinary tract instrumentation

Interstitial Cystitis (Painful Bladder or Bladder Pain Syndrome)

Definition
- bladder pain, chronic urgency and frequency without other reasonable causation

Classification
- non-ulcerative (more common)
- ulcerative

Etiology
- unknown
  - theories: increased epithelial permeability, autoimmune, neurogenic, defective GAG layer overlying mucosa

Epidemiology
- prevalence: 20/100,000
- 90% of cases are in females
- mean age at onset is 40 yr (non-ulcerative tends to affect a younger to middle-aged population, while ulcerative tends to be seen in middle-aged to older)

Clinical Features
- bladder pain, increase with filling and relief with emptying
- glomerulations (submucosal petechiae) or Hunner's lesions (ulcers) on cystoscopic examination
- urinary urgency
- negative U/A, urine C&S, and urine cytology

Cystoscopic evaluation is not necessary to make a diagnosis

Differential Diagnosis
- UTI, vaginitis, bladder tumour
- radiation/chemical/eosinophilic/TB cystitis
- eosinophilic/TB cystitis
- bladder calculi

Investigations
- Hx, P/E, urinalysis with microscopy

Four Symptom Scores Exist to Evaluate and Monitor Patients with Interstitial Cystitis
- Interstitial Cystitis Symptom Index (ICSI)
- Interstitial Cystitis Problem Index (ICPI)
- Wisconsin Interstitial Cystitis (UW-IC) Scale
- Pain, Urgency and Frequency (PUF) Score

Treatment
- first-line: patient empowerment (diet, lifestyle, stress management), pain management
- second-line
  - oral: pentosan polysulfate sodium, amitriptyline, cimetidine, hydroxyzine
  - intravesical: dimethylsulfoxide (DMSO), heparin, lidocaine
- third-line: cystoscopy with bladder hydrodistention (traditionally diagnostic) under GA, treat Hunner's lesions if present
- other: neuromodulation, cyclosporine A, intradetrusor botulinum toxin
- surgery (last resort): augmentation cystoplasty, or urinary diversion ± cystectomy

Acute Pyelonephritis

Definition
- infection of the renal parenchyma with local and systemic manifestations
- clinical diagnosis of flank pain, fever and elevated WBC

Etiology
- ascending (usually GN bacilli) or hematogenous route (usually GP cocci)
- causative microorganisms
  - gram positives: *Enterococcus faecalis, S. aureus, S. saphrophyticus*
  - gram negatives: ***E. coli***, *Klebsiella, Proteus, Pseudomonas, Enterobacter*
- common underlying causes of pyelonephritis
  - stones, strictures, prostatic obstruction, vesicoureteric reflux, neurogenic bladder, catheters, DM, sickle-cell disease, PCKD, immunosuppression, post-renal transplant, instrumentation, pregnancy

Clinical Features
- rapid onset (<24 h)
- LUTS including frequency, urgency, hematuria; NOT dysuria unless concurrent cystitis
- fever, chills, nausea, vomiting, myalgia, malaise
- CVA tenderness and/or exquisite flank pain

Investigations
- U/A, urine C&S
- CBC and differential: leukocytosis, left shift
- imaging indicated if suspicious of complicated pyelonephritis or symptoms do not improve with 48-72 h of treatment
  - abdominal/pelvic U/S
  - CT
- nuclear medicine: DMSA scan can be used to help secure the diagnosis
  - a photopenic defect indicates active infection or scar; if normal alternative diagnoses should be considered

Treatment
- hemodynamically stable
  - outpatient oral ABx treatment ± single initial IV dose (see Table 9, U12)
- severe or non-resolving
  - admit, hydrate, and treat with IV ABx (see Table 9, U12)
- emphysematous pyelonephritis
  - most patients receive nephrectomy after IV ABx started and patient stabilized
  - consider temporization with nephrostomy tubes
- renal obstruction
  - admit for emergent stenting or percutaneous nephrostomy tube

Cystoscopic evaluation is not necessary to make a diagnosis. Nitrofurantoin has poor tissue penetration and therefore is not used to treat pyelonephritis (requires post-renal uroconcentration)

Prostatitis/Prostatodynia

Epidemiology
- most common urologic diagnosis in men <50 yr
- prevalence 2-12%

Classification

Table 10. Comparison of the Three Types of Prostatitis

	Category I: Acute Bacterial Prostatitis	Category II: Chronic Bacterial Prostatitis	Category III: Chronic Pelvic Pain Syndrome (CPPS) (Abacterial)
Etiology	Ascending urethral infection with KEEPS: 80% *E. coli* Often associated with outlet obstruction, recent cystoscopy, prostatic biopsy Most infections occur in the peripheral zone (see Figure 7, U7)	Recurrent exacerbations of acute prostatitis-like signs and symptoms Recurrent UTI with same organism	Divided into inflammatory (IIIA) and non-inflammatory (IIIB) Intraprostatic reflux of urine ± urethral hypertonia Multifactorial (immunological, neuropathic, neuroendocrine, psychosocial)
Clinical Features	Acute onset fever, chills, malaise Rectal, lower back, and perineal pain LUTS	Pelvic pain, storage LUTS, ejaculatory pain, post-ejaculatory pain	Pelvic pain, storage LUTS, ejaculatory pain, post-ejaculatory pain
Investigations	P/E: abdomen, external genitalia, perineum, prostate U/A Blood CBC, C&S Transrectal U/S if non-resolving/suspect prostatic abscess	E: as per Category I + pelvic floor Urine C&S: 4-glass test VB1 (voided bladder): initial (urethra) P/VB2: midstream (bladder) EPS (expressed prostatic secretions): not usually performed VB3: post-massage/DRE	Same as per Category II NIH-CPSI score* Consider psychological assessment
Treatment	Supportive measures PO or IV ABx depending how sick (see Table 9, U12) May consider catheterization in patients with severe obstructive LUTS or retention Diagnose and treat if abscess is present	ABx (see Table 9, U12) Consider addition of an β-blocker	Supportive measures Trial of ABx therapy if newly diagnosed Multimodal treatment strategy may include: β-blocker Anti-inflammatories Phytotherapy (quercetin, cernilton)

*NIH-CPSI: National Institute of Health Chronic Prostatitis Symptom Index

4-Glass Test: Prostatic source is suggested when colony counts in EPS and VB3 exceed those of VB1 and VB2 by 10x

It is not recommended to do a serum PSA during acute bacterial prostatitis

Prostatic massage may cause extreme tenderness and increased risk of inducing sepsis, abscess, or epididymo-orchitis

Epididymitis and Orchitis

Etiology
- common infectious causes
  - <35 yr: *N. gonorrhoeae* or *Chlamydia trachomatis*
  - ≥35 yr or penetrative anal intercourse: GI organisms (especially *E. coli*)
- other causes
  - mumps infection may involve orchitis, post-parotitis
  - TB
  - syphilis
  - granulomatous (autoimmune) in elderly men
  - amiodarone (involves only head of epididymis)
  - chemical: reflux of urine into ejaculatory ducts

Risk Factors
- UTI
- unprotected sexual contact
- instrumentation/catheterization
- increased pressure in prostatic urethra (straining, voiding, heavy lifting) may cause reflux of urine along vas deferens → sterile epididymitis
- immunocompromise

Clinical Features
- sudden onset scrotal pain and swelling ± radiation along cord to flank
- scrotal erythema and tenderness
- fever
- storage symptoms, purulent d/c
- reactive hydrocele

Investigations
- U/A, urine C&S
- ± urethral d/c: Gram stain/culture
- if diagnosis uncertain, MUST rule out testicular torsion (U/S Doppler)

Treatment
- rule out torsion (see *Investigations* Table 24, U29)
- see Table 9, U12 for ABx therapy
- scrotal support, bed rest, ice, analgesia

Complications
- if severe → testicular atrophy
- 30% have persistent infertility problems

If unsure between diagnoses of epididymitis and torsion, always go to OR
Remember: torsion >6 h has poor prognosis

Prehn's Sign: pain may be relieved with elevation of testicles in epididymitis but not in testicular torsion (poor sensitivity, especially in children)

Inadequately treated acute epididymitis may lead to chronic epididymitis or epididymo-orchitis

Urethritis

Etiology
- infectious or inflammatory (e.g. reactive arthritis)

Table 11. Infectious Urethritis: Gonococcal vs. Non-Gonococcal

	Gonococcal	Non-Gonococcal
Causative Organism	*Neisseria gonorrhoeae*	Usually *Chlamydia trachomatis*
Diagnosis	Hx of sexual contact, thick, profuse, yellow-grey purulent d/c, LUTS Gram stain (GN diplococci), urine PCR and/or culture from urethral specimen	Hx of sexual contact, mucoid whitish purulent d/c, ± storage LUTS Gram stain demonstrates >4 PMN/oil immersion field, no evidence of *N. gonorrhoeae*, urine PCR and/or culture from urethral specimen
Treatment	See Table 9, U12	See Table 9, U12

Reactive Arthritis (formerly known as Reiter's syndrome)
Urethritis, uveitis (or conjunctivitis), and arthritis
(can't pee, can't see, can't climb a tree)

If culture negative or unresponsive to treatment consider: *Ureaplasma urealyticum, Mycoplasma genitalium, Trichimonas vaginalis*, HSV, or adenovirus

Stone Disease

Epidemiology
- prevalence: ~8% and increasing
- M:F = 2:1
- peak incidence 30-50 yr of age
- recurrence rate: 10% at 1 yr, 50% at 5 yr, 60-80% lifetime

Risk Factors
- hereditary: RTA, Glucose-6-phosphate dehydrogenase deficiency, cystinuria, xanthinuria, oxaluria, etc.
- lifestyle: minimal fluid intake; excess vitamin C, oxalate, purines, calcium
- medications: loop diuretics (furosemide, bumetanide), acetazolamide, topiramate, zonisamide, indinavir, acyclovir, sulfadiazine, triamterene
- medical conditions: UTI (with urea-splitting organisms: *Proteus, Pseudomonas, Providencia, Klebsiella, Mycoplasma, Serratia, S. aureus*), myeloproliferative disorders, IBD, gout, DM, hypercalcemia disorders (hyperparathyroidism, tumour lysis syndrome, sarcoidosis, histoplasmosis), obesity (BMI >30)

Key Points in Stone Hx
- Diet (especially FLUID INTAKE)
- Predisposing medical conditions
- Predisposing medications
- Previous episodes/investigations/ treatments
- Family Hx (1st degree relative)

Clinical Features
- urinary obstruction → upstream distention → pain
  - flank pain from renal capsular distention (non-colicky)
  - severe waxing and waning pain radiating from flank to groin, testis, or tip of penis from distended collecting system or ureter (ureteral colic)
- writhing, persistent discomfort, nausea, vomiting, hematuria (90% microscopic), diaphoresis, tachycardia, tachypnea
- occasionally symptoms of trigonal irritation (frequency, urgency)
- bladder stones result in: storage and voiding LUTS, terminal hematuria, suprapubic pain
- if fever, rule out concurrent pyelonephritis and/or obstruction

The four narrowest passage points for upper tract stones are:
- UPJ
- Pelvic brim
- Under vas deferens/broad ligament
- UVJ

Table 12. Differential Diagnosis of Renal Colic

GU	Abdominal	Neurological
Pyelonephritis Ureteral obstruction from other cause: UPJ obstruction, clot colic secondary to gross hematuria, sloughed papillae Gynecological: ectopic pregnancy, torsion/rupture of ovarian cyst, PID	AAA Bowel ischemia Pancreatitis Other acute abdominal crisis (appendicitis, cholecystitis, diverticulitis)	Radiculitis (L1): herpes zoster, nerve root compression

Location of Stones
- calyx: may cause flank discomfort, persistent infection, persistent hematuria, or remain asymptomatic
- pelvis: tend to cause obstruction at UPJ, may cause persistent infection
- ureter: <5 mm diameter will pass spontaneously in 75% of patients

	Radiopaque	Radiolucent
KUB	Calcium Struvite Cystine	Uric acid Indinavir Atazanavir
CT	Calcium Struvite Cystine Uric acid	Indinavir Atazanavir

Stone Pathogenesis
- supersaturation of stone constituents (at appropriate temperature and pH)
- stasis, low flow, and low volume of urine (dehydration)
- crystal formation and stone nidus
- loss of inhibitory factors
  - citrate (forms soluble complex with calcium)
  - magnesium (forms soluble complex with oxalate)
  - pyrophosphate
  - Tamm-Horsfall glycoprotein

Approach to Renal Stones

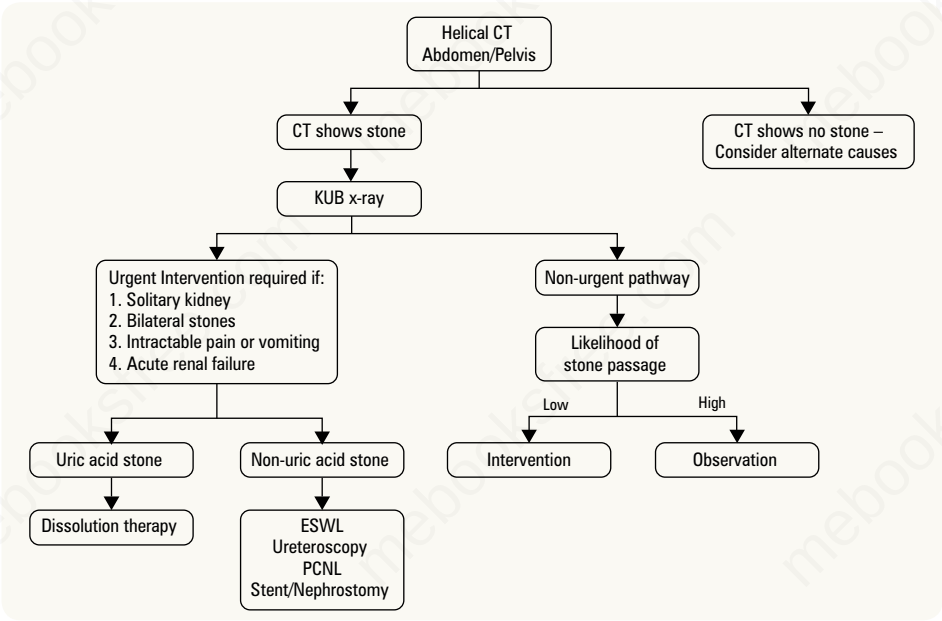


Figure 8. Approach to renal stone

Although hypercalciuria is a risk factor for stone formation, decreasing dietary calcium is NOT recommended to prevent stone formation. Low dietary calcium leads to increased GI oxalate absorption and higher urine levels of calcium oxalate

Stones and Infection
If septic, urgent decompression via ureteric stent or percutaneous nephrostomy is indicated. Definitive treatment of the stone should be delayed until the sepsis has cleared

Indications for PCNL
- Size >2 cm
- Staghorn
- UPJ obstruction with correction of obstruction
- Calyceal diverticulum
- Cystine stones (poorly fragmented with ESWL)
- Anatomical abnormalities
- Failure of less invasive modalities

Investigations

Table 13. Investigations for Renal Stones

	CBC, Uric Acid, U/A, Urine C&S	KUB x-ray	CT Scan	Abdominal Ultrasound	Cystoscopy	PTH, 24 h urine x 2 for volume, Cr, Ca^{2+}, Na^{+}, PO_4^{3-}, Mg^{2+}, oxalate, citrate, ± cystine
Who gets it?	Everyone	Most	First episode renal colic	Pediatric cases or those concerning for obstruction	± Those concerning for bladder stone	Recurrent Ca^{2+} stone formers ± pediatric cases
Why is it done?	May show signs of infection, ± sensitivities	90% of stones are radiopaque Good for follow-up	Distinguish radiolucent stone from soft tissue filling defect X-ray comparison	Identify and follow-up stone without radiation exposure Visualize hydronephrosis	Visualize bladder	Need to rule out metabolic cause for stones
Cautions	—	Do not mistake phleboliths for stones!	Radiation (especially if female of child bearing age) Must be a non-contrast scan	—	—	—

Treatment – Acute

- medical
  - analgesic ± antiemetic
  - NSAIDs help lower intra-ureteral pressure
  - medical expulsion therapy (MET)
    - α-blockers: increase rate of spontaneous passage in distal ureteral stones
  - ± Abx for bacteriuria
  - IV fluids if vomiting (note: IV fluids do NOT promote stone passage)
- interventional
  - required if obstruction endangers patient, e.g. sepsis, renal failure
  - first line: ureteric stent (via cystoscopy)
  - second line: image-guided percutaneous nephrostomy
- admit if necessary
  - see *Indications for Admission to Hospital*

Treatment – Elective

- medical
  - likely conservative if ureteral stone <10 mm or kidney stone <5 mm and no complications/symptoms well controlled
    - stones <5 mm especially likely to pass spontaneously
  - PO fluids to increase urine volume to >2 L/d (3-4 L if cystine) and MET
  - specific to stone type (see Table 14)
  - periodic imaging to monitor stone position and assess for hydronephrosis
  - progress to interventional stone removal methods if symptoms worsen or fail to improve (indicating stone passage)

24 h urine collections must be done AFTER discontinuing stone preventing/promoting medications

Indications for Admission to Hospital
- Intractable pain
- Intractable vomiting
- Fever (suggests infection)
- Compromised renal function (including single kidney, bilateral obstructing stone)
- Pregnancy

Detailed metabolic studies are NOT recommended unless complex patient (recurrent stone formers, pregnancy, pediatrics, strong family Hx, underlying kidney or systemic disease, etc.)

- interventional
  - kidney
    - may stent prior to ESWL if stone is 1.5-2.5 cm
    - ESWL if stone <2 cm
    - PCNL if stone >2 cm
  - ureteral stones >10 mm
    - ESWL and URS are both first line treatment modalities for all locations
      - URS has significantly greater stone-free rates for stones at all locations in ureter, but also has higher complication rates (ureter perforation, stricture formation, etc.)
    - PCNL is second line treatment
    - laparoscopic or open stone removal (very rare)
  - bladder
    - transurethral stone removal or cystolitholapaxy
    - remove outflow obstruction (TURP or stricture dilatation)

Prevention

- dietary modification
  - increase fluid (>2 L/d), K^+ intake
  - reduce animal protein, oxalate, Na^+, sucrose, and fructose intake
  - avoid high-dose vitamin C supplements
- medications
  - thiazide diuretics for hypercalciuria
  - allopurinol for hyperuricosuria
  - potassium citrate for hypocitraturia, hyperuricosuria

Alpha-blockers as Medical Expulsive Therapy for Ureteral Stones
Cochrane DB Syst Rev 2014;4:CD008509
Purpose: To determine whether or not α-blockers compared with other pharmacological treatments or placebo improve stone clearance rates and other clinically relevant outcomes in patients presenting with symptoms of stones less than 10 mm confirmed by imaging.
Results/Conclusions: 32 RCTs, 5,864 participants. Although patients using α-blockers were more likely to experience adverse effects compared to standard therapy, stone-free rates were significantly higher in the α-blocker group (RR 1.48, 95% CI 1.33-1.64), expulsion time was 2.91 days shorter, and there was a reduction in the number of pain episodes (MD -0.48, 95% CI -0.94 to -0.01), the need for analgesic medication (MD -38.17, 95% CI -74.93 to -1.41), and hospitalization (RR 0.35, 95% CI 0.13-0.97). α-blockers should therefore be offered as a primary treatment modality for ureteral stones.

Consideration must be given to monitoring stone formers with periodic imaging (i.e. at year 1 and then q2-4yr based on likelihood of recurrence)

Table 14. Stone Classification

Type of Stone	Calcium (75-85%)	Uric Acid (5-10%)	Struvite (5-10%)	Cystine (1%)
Etiology	Hypercalciuria Hyperuricosuria (25% of patients with Ca^{2+} stones) Hyperoxaluria (<5% of patients) Hypocitraturia (12% of patients) Other causes: Hypomagnesemia – associated with hyperoxaluria and hypocitraturia High dietary Na^+ Decreased urinary proteins High urinary pH, low urine volume (e.g. GI water loss) Hyperparathyroidism, obesity, gout, DM	Uric acid precipitates in low volume, acidic urine with a high uric acid concentration: Hyperuricosuria alone Drugs (ASA, thiazides) Diet (purine rich red meats) Hyperuricosuria with hyperuricemia Gout High rate of cell turnover or cell death (leukemia, cytotoxic drugs)	Infection with urea-splitting organisms (*Proteus, Pseudomonas, Providencia, Klebsiella, Mycoplasma, Serratia, S. aureus*) results in alkaline urinary pH and precipitation of struvite (magnesium ammonium phosphate)	Autosomal recessive defect in small bowel mucosal absorption and renal tubular absorption of dibasic amino acids results in "COLA" in urine (cystine, ornithine, lysine, arginine)
Key Features	Radiopaque on KUB Reducing dietary Ca^{2+} is NOT an effective method of prevention/treatment	Radiolucent on KUB Radiopaque on CT Acidic urine, pH <5.5 (NOT necessarily elevated urinary uric acid)	Perpetuates UTI because stone itself harbours organism Stone and all foreign bodies must be cleared to avoid recurrence Associated with staghorn calculi Positive urine dip and cultures Note: *E. coli* infection does not cause struvite stones M:F = 3:1, UTI more common in female	Aggressive stone disease seen in children and young adults Recurrent stone formation, family Hx Often staghorn calculi Faintly radiopaque on KUB Positive urine sodium nitroprusside test, urine chromatography for cystine
Treatment Medical if stone <5 mm and no complications Procedural/Surgical treatment if stone >5 mm or presence of complications	Fluids to increase urine volume to >2 L/d For calcium stones: cellulose phosphate, orthophosphate for absorptive causes Calcium oxalate: thiazides, ± potassium citrate, ± allopurinol Calcium struvite: ABx (stone must be removed to treat infection)	Increased fluid intake Alkalinization of urine to pH 6.5 to 7 (bicarbonate, potassium citrate) ± allopurinol	Complete stone clearance ABx for 6 wk Regular follow-up urine cultures	Increased fluid intake (3-4 L of urine/d) Alkalinize urine (bicarbonate, potassium citrate), Penicillamine/α-MPG or Captopril (form complex with cystine) ESWL not effective

Urological Neoplasms

Approach to Renal Mass

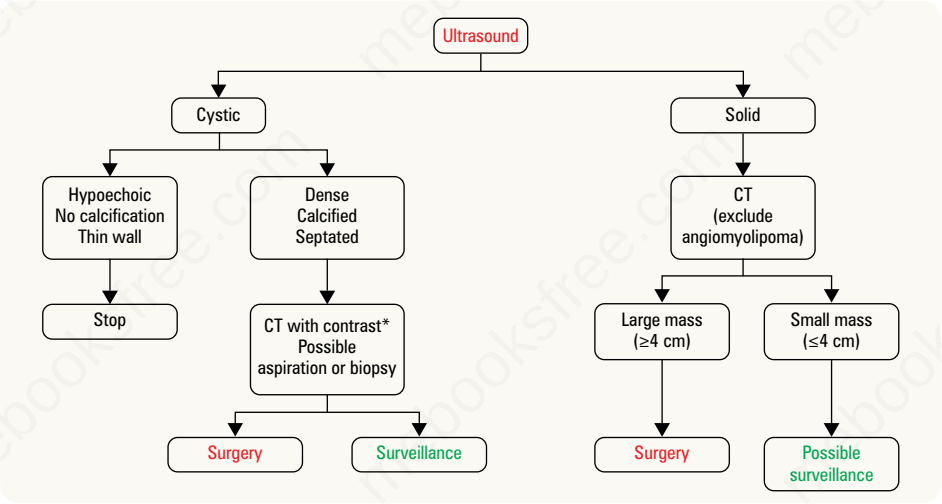


Figure 9. Workup of a renal mass
*Imaging modality may be different in cases of contrast allergy or elevated creatinine

There is controversy over optimal management of small renal masses

Percutaneous needle biopsies of cystic renal masses may lead to peritoneal seeding

Tuberous Sclerosis
- Syndrome characterized by mental retardation, epilepsy, and adenoma sebaceum
- 45-80% of patients also present with angiomyolipomas which are often multiple and bilateral

Benign Renal Neoplasms

CYSTIC KIDNEY DISEASE

- simple cysts: usually solitary or unilateral
  - very common: up to 50% at age 50
  - usually incidental finding on abdominal imaging
  - Bosniak Classification is used to stratify for risk of malignancy based on cyst features from contrast CT
- polycystic kidney disease
  - autosomal recessive: multiple bilateral cysts, often leading to early renal failure in infants
  - autosomal dominant: progressive bilateral disease leading to HTN and renal failure, adult-onset
- medullary sponge kidney: cystic dilatation of the collecting ducts
  - usually benign course, but patients are predisposed to stone disease
- von Hippel-Lindau syndrome: multiple bilateral cysts or clear cell carcinomas (50% incidence of RCC)
  - renal cysts, cerebellar, spinal and retinal hemangioblastomas, pancreatic and epididymal cysts, pheochromocytomas

Table 15. Bosniak Classification of Renal Cysts

Class	Description	Features	Risk of Malignancy	Management Plan
I	Simple cyst	Round, no septations, no calcifications, no solid component	Near zero	Follow-up usually not required
II	Simple cyst	A few thin septa, no true enhancement, well-marginated, uniform high attenuation, <3 cm	Minimal	Follow-up usually not required
IIF	Minimally complex cyst with extra features that require follow-up	Still well-marginated and non-enhancing, but now multiple thin septa or some thickening/calcification of septa/wall, >3 cm	5-20%	Requires follow-up with imaging q6-12mo If the lesion evolves, may require surgical resection
III	Complex cyst	Thicker or more irregular walls with measurable enhancement	>50%	Requires surgical resection
IV	Clearly malignant	Class III + enhancing soft-tissue components	>90%	Requires surgical resection

Table 16. Benign Renal Masses

	Angiomyolipoma (Renal Hamartoma)	Renal Oncocytoma	Renal Adenoma
Epidemiology	<1% of adult renal tumours F>M 20% associated with tuberous sclerosis (especially if multiple, recurrent)	3-7% of renal tumours M>F Oncocytomas also found in adrenal, thyroid and parathyroid glands	Most common benign renal neoplasm M:F = 3:1 Incidence increases with age Found in 7-23% of all autopsies
Characteristics	Clonal neoplasm consisting of blood vessels (angio-), smooth muscle (-myo-), and fat (-lipoma) May extend into regional lymphatics and other organs and become symptomatic	Spherical, capsulated with possible central scar Histologically organized aggregates of eosinophilic cells originating from intercalated cells of collecting duct	Small cortical lesions <1 cm Majority are solitary but can be multifocal
Diagnosis	Incidental finding on CT Negative attenuation (-20 HU) on CT is pathognomonic Rare presentation of hematuria, flank pain, and palpable mass (same as RCC)	Incidental finding on CT Difficult to distinguish from RCC on imaging – treated as RCC until proven otherwise Biopsy may be performed to rule out malignancy	Incidental finding on CT Rarely symptomatic Controversy as to whether this represents benign or pre-malignant neoplasm
Management	May consider surgical excision or embolization if symptomatic (pain, bleeding) or higher risk of bleeding (e.g. pregnancy) Potential role for mTOR inhibitors in unresectable/ metastatic disease Follow with serial U/S	Partial/radical nephrectomy for large masses HIFU or RFA for smaller masses	If mass >3 cm, likely not a benign adenoma; will require partial/radical nephrectomy due to increased likelihood of malignancy

Malignant Renal Neoplasms

RENAL CELL CARCINOMA

Etiology
- cause unknown
- originates from proximal convoluted tubule epithelial cells in clear cell subtype (most common)
- hereditary forms seen with von Hippel-Lindau syndrome and hereditary papillary renal carcinoma

Epidemiology
- 85% of primary malignant tumours in kidney
- M:F = 1.5:1
- peak incidence at 50-60 yr of age

Pathology
- histological subtypes: clear cell (75-85%), papillary (10-15%), chromophobic (5-10%), collecting duct
- sarcomatoid elements in any subtype is a marker of poor prognosis

Risk Factors
- top 3 risk factors: smoking, HTN, obesity
- miscellaneous: horseshoe kidney, acquired renal cystic disease
- role of environmental exposures (aromatic hydrocarbons, etc.) remains an unproven risk factor for development of RCC

Clinical Features
- usually asymptomatic: frequently diagnosed incidentally by U/S or CT
- indicators for poor prognosis: weight loss, weakness, anemia, bone pain
- classic "too late triad" found in 10-15%
  - gross hematuria 50%
  - flank pain <50%
  - palpable mass <30%
- metastases: seen in a 1/3 of new cases; additional 20-40% will go on to develop metastases (mostly in late presentations or large tumours)
  - bone, brain, lung and liver most common site
  - may invade renal veins and IVC lumen. This may result in ascites, hepatic dysfunction, right atrial tumour, and pulmonary emboli

Investigations
- routine labs for paraneoplastic syndromes (CBC, ESR, LFTs, extended electrolytes)
- U/A
- renal U/S: solid vs. cystic lesion
- contrast-enhanced CT: higher sensitivity than U/S for detection of renal masses and for staging purposes
- MRI: useful for evaluation of vascular extension
- renal biopsy: to confirm diagnosis if considering observation or other non-surgical therapy

Staging
- involves CT, CXR, liver enzymes and LFTs, bone/head imaging (if symptoms dictate)

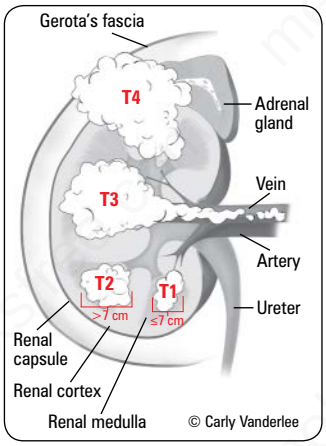


Figure 10. RCC staging

Role of environmental exposures (aromatic hydrocarbons, etc.) remains an unproven risk factor for development of RCC

RCC Systemic Effects: paraneoplastic syndromes (10-40% of patients)
- Hematopoietic disturbances: anemia, polycythemia, raised ESR
- Endocrinopathies: hypercalcemia (increased vitamin D hydroxylation), erythrocytosis (increased erythropoietin), HTN (increased renin), production of other hormones (prolactin, gonadotropins, TSH, insulin, and cortisol)
- Hepatic cell dysfunction or Stauffer syndrome: abnormal LFTs, decreased WBC count, fever, areas of hepatic necrosis; no evidence of metastases; reversible following removal of primary tumour
- Hemodynamic alterations: systolic HTN (due to AV shunting), peripheral edema (due to caval obstruction)

Tumour may invade renal veins and inferior vena cava lumen. This may result in ascites, hepatic dysfunction, right atrial tumour, and pulmonary emboli

Table 17. 2010 TNM Classification of Renal Cell Carcinoma

T	N	M
T1: tumour <7 cm, confined to renal parenchyma	**N0**: no regional lymph node metastasis	**M0**: no evidence of metastasis
T1a: <4 cm	**N1**: metastasis in regional lymph nodes	**M1**: presence of distant metastasis
T1b: 4-7 cm		
T2: tumour >7 cm, confined to renal parenchyma		
T2a: 7-10 cm		
T2b: >10cm		
T3: tumour extends into major veins or perinephric tissues, but NOT into ipsilateral adrenal or beyond Gerota's fascia		
T3a: into renal vein or sinus fat		
T3b: into infradiaphragmatic IVC		
T3c: into supradiaphragmatic IVC		
T4: tumour extends beyond Gerota's fascia including extension into ipsilateral adrenal		

Treatment
- surgical
  - radical nephrectomy: en bloc removal of kidney, tumour, ipsilateral adrenal gland (in upper pole tumours) and intact Gerota's capsule and paraaortic lymphadenectomy
  - partial nephrectomy (parenchyma-sparing): small tumour (roughly <4 cm) or solitary kidney/bilateral tumours
  - surgical removal of solitary metastasis may be considered
- ablative techniques (cryoablation, RFA)
- palliative radiation to painful bony lesions
- therapy for advanced stage
  - tyrosine kinase inhibitors for metastatic disease (e.g. sunitinib, sorafenib)
  - anti-angiogenesis/anti-VEGF (e.g. bevacizumab)
  - mTOR inhibitors (e.g. temsirolimus, everolimus)
  - high-dose IL-2 (high toxicity but able to induce long-term cure in 5-7% of patients)
  - IFN-α: monotherapy has been largely replaced by molecularly targeted agents listed above

Prognosis
- stage at diagnosis most important prognostic factor
  - T1: 90-100% 5 yr survival
  - T2-T3: 60% 5 yr survival
  - metastatic disease: <5% 10 yr survival

Carcinoma of the Renal Pelvis and Ureter

Etiology
- risk factors include:
  - smoking
  - chemicals/dietary exposures (industrial dyes and solvents; aristolochic acid, aniline dyes)
  - analgesic abuse (acetaminophen, ASA, and phenacetin)
  - Balkan nephropathy

Epidemiology
- rare: accounts for 5% of all urothelial cancers
- frequently multifocal, 2-5% are bilateral
- M:F = 3:1
- relative incidence: bladder:renal:ureter = 100:10:1

Pathology
- 85% are papillary urothelial carcinoma; others include SCC and adenocarcinoma
- UCC of ureter and renal pelvis are histologically similar to bladder UCC

Clinical Features
- gross/microscopic hematuria
- flank pain
- storage or voiding symptoms (dysuria only if lower urinary tract involved)
- flank mass ± hydronephrosis (10-20%)

Carcinoma: Final Efficacy of Safety Results of the Phase III Treatment Approaches in Renal Cancer Global Evaluation Trial
J Clin Oncol 2009; 27(20):3312-8.
Purpose: Phase III trial of renal cell carcinoma patients who were randomized to receive either sorafenib (n=451) or placebo (n=452).
Results: The overall survival was 17.8 months in the treatment group, compared to 15.2 months in the control group (HR = .88, p =.146). Following adjustment for crossover patients (from placebo to treatment), a significant difference was found in the overall survival (17.8 vs. 14.3 months, HR = .78, p = .029). No difference was found in adverse events at 16 months.

Axitinib vs. Sorafenib as Second-Line Treatment for Advanced Renal Cell Carcinoma: Overall Survival Analysis and Updated Results from a Randomized Phase 3 Trial
Lancet Oncol 2013;14:552-562
Study: Phase 3 trial of patients with clear cell metastatic renal cell carcinoma randomized to receive axitinib 5 mg twice daily (n=361) or sorafenib 400 mg twice daily (n=362).
Results: Median overall survival was 20.1 mo with axitinib (16.7 -23.4) and 19.2 mo with sorafenib (17.5-22.3) (HR 0.969, 95% CI 0.800-1.174). Median progression-free survival was 8.3 mo with axitinib (6.7-9.2) and 5.7 mo with sorafenib (4.7-6.5) (HR 0.656, 95% CI 0.552-0.779).
Conclusions: Axitinib should be a second-line treatment option for patients with metastatic renal cell carcinoma.

Radiotherapy With or Without Chemotherapy in Muscle-Invasive Bladder Cancer
NEJM 2012;366:1477-1488
Study: Phase 3 trial with random assignment of 360 patients with muscle-invasive bladder cancer to radiotherapy with or without chemotherapy.
Results: At 2 yr, rates of locoregional disease-free survival were 67% in the chemoradiotherapy group and 54% in the radiotherapy group (HR 0.68, 95% CI 0.48-0.96). Five year overall survival rates were 48% in the chemoradiotherapy group and 35% in the radiotherapy group (HR 0.82, 95% CI 0.63-1.09).
Conclusions: Chemotherapy with fluorouracil and mitomycin C in combination with radiotherapy improves locoregional control of bladder cancer compared to radiotherapy alone, with no significant increase in adverse events.

Differential Diagnosis of Filling Defect
- Urothelial carcinoma (differentiate via cytology and CT scan)
- Uric acid stone (differentiate via cytology and CT scan)
- Blood clot
- Pyelitis cystica
- Papillary necrosis
- Fungus ball
- Gas bubble from gas producing organisms

Investigations
- IVP/CT urogram
- cystoscopy and retrograde pyelogram

Treatment
- radical nephroureterectomy with excision of ipsilateral bladder cuff
- distal ureterectomy for distal ureteral tumours with concomitant ureteral reimplant
- emerging role for endoscopic laser ablation in patients with low grade disease, poor baseline renal health

Bladder Carcinoma

Etiology
- unknown, but environmental risk factors include:
  - smoking (main factor – implicated in 60% of new cases)
  - aromatic amines: naphthylamines, benzidine, tryptophan, phenacetin metabolites
  - cyclophosphamide
  - prior Hx of radiation treatment to the pelvis
  - *Schistosoma hematobium* infection (associated with SCC)
  - chronic irritation: cystitis, chronic catheterization, bladder stones (associated with SCC)
  - aristolochic acid: associated with Balkan Nephropathy (renal failure, upper tract urothelial cancer) and Chinese Herbal Nephropathy

The "field defect" theory helps to explain why UCC has multiple lesions and has a high recurrence rate. The entire urothelium (pelvis to bladder) is bathed in carcinogens

Epidemiology
- 2nd most common urological malignancy
- M:F = 3:1, more common among whites than blacks
- mean age at diagnosis is 65 yr

Pathology
- classification
  - urothelial carcinoma (UC) >90%
  - SCC 5-7%
  - adenocarcinoma 1%
  - others <1%
- stages and prognoses of urothelial carcinoma at diagnosis
  - non-muscle invasive (75%) → >80% overall survival
    - 15% of these will progress to invasive UC
    - majority of these patients will have recurrence
  - invasive (25%) → 50-60% 5 yr survival
    - 85% have no prior history of superficial UC (i.e. *de novo*)
    - 50% have occult metastases at diagnosis, and most of these will develop overt clinical evidence of metastases within 1 yr – lymph nodes, lung, peritoneum, liver
- carcinoma *in situ* → flat, non-papillary erythematous lesion characterized by dysplasia confined to urothelium
  - more aggressive, worse prognosis
  - usually multifocal
  - may progress to invasive UCC

The ENTIRE urinary tract must be evaluated in patients with hematuria unless there is clear evidence of glomerular bleeding (e.g. red cell casts, dysmorphic RBCs, etc.)

Cystoscopy is the initial procedure of choice for the diagnosis and staging of urothelial malignancy

Unexplained hematuria in any individual >40 yr old must be investigated to rule out a malignancy

Tumour grade is the single most important prognostic factor for progression

Clinical Features
- asymptomatic (20%)
- hematuria (key symptom: 85-90% at the time of diagnosis)
- pain (50%) → location determined by size/extent of tumour (i.e. flank, suprapubic, perineal, abdominal, etc.)
- clot retention (17%)
- storage urinary symptoms → consider carcinoma *in situ*
- palpable mass on bimanual exam → likely muscle invasion
- obstruction of ureters → hydronephrosis and uremia (nausea, vomiting, and diarrhea)

Investigations
- U/A, urine C&S, urine cytology
- U/S
- CT scan with contrast → look for filling defect
- cystoscopy with biopsy (gold standard) → establish diagnosis and to determine depth of penetration
- specific bladder tumour markers (e.g. NMP-22, BTA, Immunocyt, FDP)

Grading
- low grade: <=10% invasive, 60% recur locally
- high grade: 50-80% are invasive or are expected to progress to invasive over time

Staging
- for invasive disease: CT or MRI, CXR, LFTs, extended electrolytes (Ca^{2+}, Mg^{2+}, PO_4^{3-}) (metastatic workup)

Non-Muscle-Invasive Bladder Cancer (NMIBC) and BCG
AHRQ Publication 2015:15-EHC017-EF #153
Summary: BCG is the only intravesical therapy associated with decreased risk of bladder cancer progression; however, it is also associated with high rate of adverse events. More research is needed to define optimal dose/regimen.
Methods: Review of Ovid Medline, Cochrane Central Register of Controlled Trials, Cochrane Database of SR, Health Technology Assessment, National Health Sciences Economic Evaluation, Database of Abstract of Review of Effects for studies on NMIBC interventions, including intravesical therapy.
Results: BCG is superior in prevention of bladder cancer recurrence compared to no intravesical therapy. BCG is superior to doxorubicin, epirubicin, and mitomycin in prevention of bladder cancer recurrence.

Table 18. 2010 TNM Classification of Bladder Carcinoma

T	N	M
TX: Primary tumour cannot be assessed **T0**: No evidence of primary tumour **Ta**: Noninvasive papillary carcinoma **Tis**: Carcinoma *in situ*: "flat tumour" **T1**: Tumour invades subepithelial connective tissue **T2**: Tumour invades muscularis propria **pT2a**: Tumour invades superficial muscularis propria (inner half) **pT2b**: Tumour invades deep muscularis propria (outer half) **T3**: Tumour invades perivesical tissue **pT3a**: Microscopically **pT3b**: Macroscopically (extravesical mass) **T4**: Tumour invades any of the following: prostatic stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall **T4a**: Tumour invades prostatic stroma, uterus, vagina **T4b**: Tumour invades pelvic wall, abdominal wall	**NX**: Lymph nodes cannot be assessed **N0**: No lymph node metastasis **N1**: Single regional lymph node metastasis in the true pelvis (hypogastric, obturator, external iliac, or presacral lymph node) **N2**: Multiple regional lymph node metastasis in the true pelvis (hypogastric, obturator, external iliac, or presacral lymph node metastasis) **N3**: Lymph node metastasis to the common iliac lymph nodes	**M0**: No distant metastasis **M1**: Distant metastasis

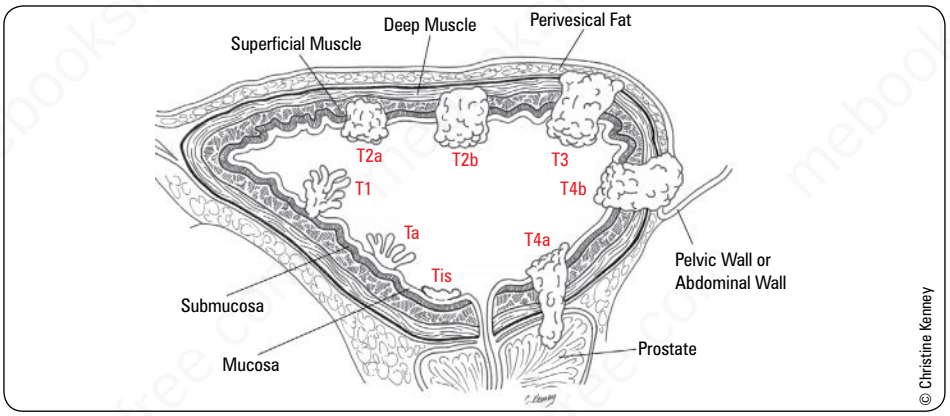


Figure 11. Urothelial carcinoma of bladder

Treatment

- superficial (non-muscle invasive) disease: Tis, Ta, T1
  - low-grade disease
    - TURBT ± intravesical chemotherapy (mitomycin C) to decrease recurrence rate
    - follow-up with cystoscopy and cytology
  - multifocal, or recurrent
    - TURBT ± intravesical chemo/immuno-therapy (e.g. BCG, mitomycin C) to decrease recurrence rate
  - T1 or CIS
    - repeat TURBT in 2-6 wk
    - maintenance with intravesical chemotherapy with BCG for 3 cycles every 3 mo, may be continued for 2-3 yr
- invasive disease: T2a, T2b, T3
  - radical cystectomy + pelvic lymphadenectomy with urinary diversion (e.g. ileal conduit, Indiana pouch, ileal neobladder) or TURBT + chemo-radiation (bladder sparing) for small tumours with non-obstructed ureters
  - neo-adjuvant chemotherapy prior to cystectomy may also be done
  - use of adjuvant chemotherapy after definitive local treatment is controversial
- advanced/metastatic disease: T4a, T4b, N^+, M^+
  - initial combination of systemic chemotherapy ± irradiation ± surgery

Prognosis

- depends on stage, grade, size, number of lesions, recurrence and presence of CIS
  - T1: 90% 5 yr survival
  - T2: 55% 5 yr survival
  - T3: 30% 5 yr survival
  - T4/N+/M+: <5% 5 yr survival

Neoadjuvant Chemotherapy plus Cystectomy Compared with Cystectomy Alone for Locally Advanced Bladder Cancer
NEJM 2003;349:859-866
Study: Randomized clinical trial.
Patients: 317 patients with transitional-cell carcinoma of the bladder (T2N0M0 to T4aN0M0).
Intervention: Randomized to undergo radical cystectomy or to receive three cycles of combined chemotherapy (methotrexate, vinblastine, doxorubicin, and cisplatin) followed by radical cystectomy.
Main Outcome: Survival. Secondary objective was to quantify down-staging of tumour following chemotherapy.
Results: At 5 yr after treatment initiation, 57% of the combination-therapy group vs. 43% of the cystectomy group were alive (p=0.06). In the combination-therapy group, 38% of the patients were pathologically free of cancer at the time of cystectomy vs. 15% of the cystectomy-only group at the time of surgery (p<0.001).
Conclusions: For locally advanced bladder carcinoma, neoadjuvant chemotherapy significantly reduces tumour volume and also improves survival.

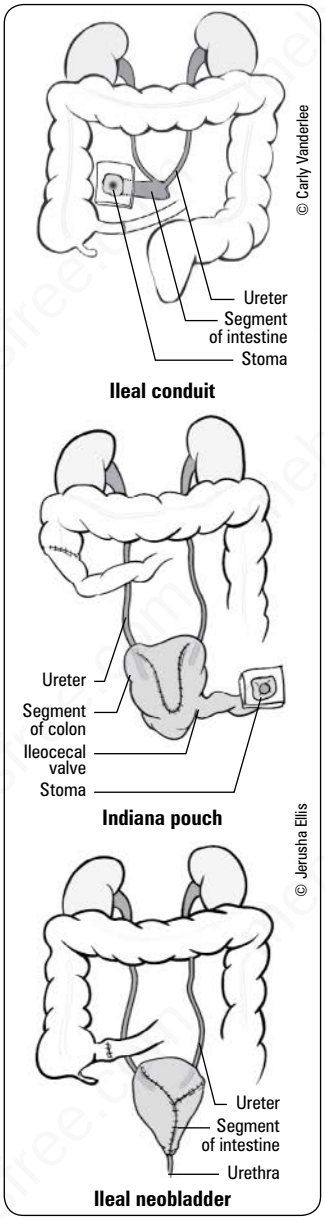


Figure 12. Ileal conduit, Indiana pouch, ileal neobladder

Prostate Cancer

Etiology
- not known
- risk factors
  - age >50 yr, risk increases 1% per year after 65 yr
  - increased incidence in persons of African descent
  - high dietary fat (2x)
  - family Hx
    - 1st degree relative (2x)
    - 1st and 2nd degree relatives (9x)
  - positive BRCA mutation

Epidemiology
- most prevalent cancer in males
- 3rd leading cause of male cancer deaths (following lung and colon)
- up to 50% risk of CaP at age 50
- lifetime risk of death from CaP is 3%
- 75% diagnosed between ages of 60 and 85; mean age at diagnosis is 65

Pathology
- adenocarcinoma
  - >95%, often multifocal
- urothelial carcinoma of the prostate (4.5%)
  - associated with UC of bladder; does NOT follow TNM staging below; not hormone-responsive
- endometrial (rare)
  - carcinoma of the utricle

Anatomy (see Figure 7, U7)
- 60-70% of nodules arise in the peripheral zone
- 10-20% arise in the transition zone
- 5-10% arise in the central zone

Clinical Features
- usually asymptomatic
- most commonly detected by DRE, elevated PSA, or as an incidental finding on TURP
  - DRE: hard irregular nodule or diffuse dense induration involving one or both lobes
  - PSA: see *Prostate Cancer Screening*, U26
- locally advanced disease
  - storage and voiding symptoms, ED (all uncommon without spread)
- metastatic disease
  - bony metastases to axial skeleton common
  - visceral metastases are less common (liver, lung, and adrenal gland most common sites)
  - leg pain and edema with nodal metastases obstructing lymphatic and venous drainage

Methods of Spread
- local invasion
- lymphatic spread to regional nodes
  - obturator > iliac > presacral/para-aortic
- hematogenous dissemination occurs early

Investigations
- DRE
- PSA elevated in the majority of patients with CaP
- TRUS-guided needle biopsy
- bone scan may be omitted in untreated CaP with PSA <10 ng/mL
- CT scanning to assess metastases
- MRI: being investigated for possible role in detection, staging, MRI-guided biopsy and active surveillance

Table 19. 2010 TNM Classification of Prostate Carcinoma

T	N	M
T1: clinically undetectable tumour, normal DRE and TRUS **T1a**: tumour incidental histologic finding in <5% of tissue resected **T1b**: tumour incidental histologic finding in >5% of tissue resected **T1c**: tumour identified by needle biopsy (due to elevated PSA level) **T2**: palpable, confined to prostate **T2a**: tumour involving ≤ one half of one lobe **T2b**: tumour involving > one half of one lobe, but not both lobes **T2c**: tumour involving both lobes **T3**: tumour extends through prostate capsule **T3a**: extracapsular extension (unilateral or bilateral) **T3b**: tumour invading seminal vesicle(s) **T4**: tumour invades adjacent structures (besides seminal vesicles)	**NX**: regional lymph nodes were not assessed **N0**: no regional lymph node metastasis **N1**: spread to regional lymph nodes	M0: no distant metastasis M: distant metastasis M1a: nonregional lymph nodes M1b: bone(s) M1c: other site(s) with or without bone disease

Table 20. Prostate Cancer Mortality Risk

	Low Risk (if any of following)	Intermediate Risk (if any of following)	High Risk (if any of following)
PSA	<10	10-20	>20
Gleason Score	<7	7	8-10
Stage	pT1-2a	pT2b-T2c	pT3/4

Treatment
- T1/T2 (localized, low-risk)
  - if adequate life expectancy or no other significant comorbidities, consider active surveillance vs. definitive local treatment (RP, brachytherapy, or EBRT)
  - active surveillance for low risk, small volume Gleason 6 prostate cancer
  - no difference in cure or recurrence rates between definitive treatment modalities
  - in older population: watchful waiting + palliative treatment for symptomatic progression
- T1/T2 (intermediate or high-risk)
  - definitive therapy over active surveillance
- T3, T4
  - EBRT + androgen deprivation therapy or RP + adjuvant EBRT
- N >0 or M >0
  - requires hormonal therapy/palliative radiotherapy for metastases; may consider combined androgen blockade
  - bilateral orchiectomy – decreases testosterone production by 90%
  - GnRH agonists (e.g. leuprolide, goserelin)
  - GnRH antagonist (e.g. degarelix)
  - estrogens (e.g. diethylstilbestrol [DES])
  - antiandrogens (e.g. bicalutamide, enzalutamide)
  - local irradiation of painful secondaries or half-body irradiation
- hormone-refractory prostate cancer
  - chemotherapy: docetaxel, cabazitaxel, sipuleucel-T

Table 21. Treatment Options for Localized Prostate Cancer

Modality	Population Considered	Limitations
Watchful Waiting	Short life expectancy (<5-10 yr); will likely only receive non-curative hormonal therapy if disease progresses	Disease progression
Active Surveillance (serial PSA, DRE, and biopsies)	Low grade disease, good follow-up; is still considering more curative treatment if disease progresses	Disease progression; decrease in QOL associated with serial testing; risks associated with biopsies; no optimal monitoring schedule has been defined to date
Brachytherapy	Low volume, low PSA (<10), low grade	ED (50%), long-term effectiveness not well-established
EBRT	Locally advanced disease, older patients	Radiation proctitis (5%), ED (50%), risk of rectal cancer
RP	Young patients (<75 yr), high-risk disease	Incontinence (10%), ED (30-50%)

*Other options include cryosurgery, HIFU, hormonal ablation

Prognosis
- T1-T2: comparable to normal life expectancy
- T3-T4: 40-70% 10 yr survival
- N^+ and/or M+: 4 % 5 yr survival
- prognostic factors: tumour stage, tumour grade, PSA value, PSA doubling time

Prostate Cancer Screening

Digital Rectal Exam
- should be included as part of initial screening
- suspicious findings: abnormal feeling, nodularity, focal lesion, discrete change in texture/fullness/symmetry

Prostate Specific Antigen
- glycoprotein produced by epithelial cells of prostate gland
- leaks into circulation in setting of disrupted glandular architecture
- value of <4 ng/mL traditionally considered as cut-off to differentiate normal from pathologic value, but no single justifiable cutpoint
- measured serum PSA is a combination of free (15%) and bound PSA (85%)
- PSA velocity, PSA density, and free:total PSA: all intended to increase sensitivity and specificity of serum PSA values
  - decreased free:total PSA, elevated PSA velocity and elevated PSA density associated with increased CaP rates

Screening Recommendations
- conflicting evidence regarding mortality reduction with PSA-based screening and debate regarding overdiagnosis/overtreatment

10 Year Outcomes After Monitoring, Surgery, or Radiotherapy for Localized Prostates Cancer
NEJM. 2016;375(15):1415-1424
Summary: At 10 years, prostate-cancer-specific mortality was low regardless of the treatment, with no significant difference among treatments. Surgery and radiotherapy were associated with lower incidences of disease progression and metastasis vs. active monitoring.
Methods: 1643 men randomized into active monitoring (545), surgery (553), and radiotherapy (545).
- Primary outcome: prostate-cancer mortality at median 10 year follow-up.
- Secondary outcomes: rate of disease progression, metastases, and all-cause deaths.

Results:
1. Primary outcome: 17 prostate-cancer-specific deaths overall; 8 in active-monitoring group, 5 in the surgery group, and 4 in the radiotherapy group; difference among the groups was not significant (p=0.48). No significant difference was seen among groups in numbers of deaths from any cause (169 deaths overall; p=0.87).
2. Secondary outcomes: metastases developed more in active monitoring group (33 men) vs. surgery group (13 men) or radiotherapy group (16 men) (overall p=0.004). Higher rates of disease progression in active-monitoring group (112 events) vs. surgery group (46 events) or radiotherapy group (46 events) (p<0.001 for the overall comparison).

Long-Term Follow-Up on PSA Screening
Lancet 2014:384(9959):2027-2035
Summary: With 13 yr follow-up, the mortality reduction remains unchanged (21%, and 29% after non-compliance adjustment). However, the number needed to screen and to treat is decreasing, and is now below the number needed to screen observed in breast cancer trials.
Methods: multi-centre RCT with predefined central database, analysis, and core age group (55-69 years) evaluating PSA in 8 European countries. Incidence and mortality truncated at 9, 11, and 13 years follow-up in the intervention arm was compared to control arm.
Results: RR of PCa incidence between intervention and control arms was 1.91 after 9 yr follow-up, 1.66 at 11 year follow-up, and 1.67 at 13 yr follow-up. RR of PCa mortality was 0.85, 0.78, and 0.79, at 9, 11, 13 yr follow-up, respectively. RRR is 21%, and ARR from death is 1.28 per 1000 men.

Causes of Increased PSA
BPH, prostatitis, prostatic ischemia/infarction, prostate biopsy/surgery, prostatic massage, acute urinary retention, urethral catheterization, cystoscopy, TRUS, strenuous exercise, perineal trauma, ejaculation, acute renal failure, coronary bypass graft, radiation therapy

PSA is specific to the PROSTATE, but NOT to prostate cancer

- Long-Term Care and United States Preventative Services Task Force all recommend against PSA testing as a population-wide screening tool
- however, serum PSA screening recommended in any man with >10 yr life-expectancy and any of the following:
  - suspicious finding on DRE
  - moderate-severe LUTS
  - high risk individuals
  - investigating secondary carcinoma of unknown origin to rule out CaP as primary

Canadian Urological Association Guidelines (2011) re: CaP Screening

- harms and benefits of PSA testing must be explained to the patient and an informed, shared decision to test must be established
- initial screening should include both serum PSA and DRE
- all men should be offered screening at age 50 if >10 yr life-expectancy
- high-risk individuals (family Hx of CaP or African ancestry) should be offered screening at age 40 if >10 yr life-expectancy
- standard has been annual screening, but q2-4yr screening acceptable
- no strict cutpoint for when to biopsy; decision to biopsy should be based on more than a single PSA value
- AUA guidelines recommend against universal routine PSA screening for CaP

Screening for Prostate Cancer
Cochrane DB Syst Rev 2013;1:CD004720
Background: Screening for prostate cancer has an unclear benefit for reducing prostate cancer-specific mortality and morbidity.
Study: Systematic review of randomized clinical trials of screening vs. no screening. A total of 31 trials were retrieved for this review.
Results: A meta-analysis of 5 RCTs with 341,342 participants was done. Collectively, there was no significant reduction in prostate cancer-specific mortality within 10 yr of follow-up. Screening procedures and biopsies were commonly associated with bleeding, bruising, and short-term anxiety; subsequent over-diagnosis and overtreatment resulted in additional harms, some severe.
Conclusions: Men who have a life expectancy less than 10-15 yr should be informed that screening for prostate cancer is unlikely to be beneficial. Significant harms are associated with screening, over-diagnosis, and overtreatment.

Testicular Tumours

Etiology/Risk Factors

- cryptorchidism, atrophy, sex hormones, HIV infection, infertility, family Hx, past Hx of testicular cancer

Epidemiology

- rare, but most common solid malignancy in young males 15-35 yr
- any solid testicular mass or acute hydrocoele in young patient – must rule out malignancy
- slightly more common in right testis (corresponds with slightly higher incidence of right-sided cryptorchidism)
- 2-3% bilateral (simultaneously or successively)

Pathology

- primary
  - 1% of all malignancies in males
  - cryptorchidism has increased risk (10-40x) of malignancy
  - 95% are germ cell tumours (all are malignant)
    - seminoma (35%) → classic, anaplastic, spermatocytic
    - NSGCT → embryonal cell carcinoma (20%), teratoma (5%), choriocarcinoma (<1%), yolk sac (<<1%), mixed cell type (40%)
  - 5% are non-germ cell tumours (usually benign) → Leydig (testosterone, precocious puberty), Sertoli (gynecomastia, decreased libido)
- secondary
  - male >50 yr
  - usually lymphoma or metastases (e.g. lung, prostate, GI)

Clinical Features

- painless testicular enlargement (painful if intratesticular hemorrhage or infarction)
- dull, heavy ache in lower abdomen, anal area or scrotum
- associated hydrocele (10%)
- coincidental trauma (10%)
- infertility (rarely presenting complaint)
- gynecomastia due to secretory tumour effects
- supraclavicular and inguinal lymphadenopathy
- abdominal mass (retroperitoneal lymph node mets)

Methods of Spread

- local spread follows lymphatics
  - right → medial, paracaval, anterior and lateral nodes
  - left → left lateral and anterior paraaortic nodes
  - "cross-over" metastases from right to left are fairly common, but no reports from left to right
- hematogenous most commonly to lung, liver, bones, and kidney

Investigations

- diagnosis is established by pathological evaluation of specimen obtained by radical inguinal orchidectomy
- tumour markers (β-hCG, LDH, AFP)
  - β-hCG and AFP are positive in 85% of non-seminomatous tumours
  - elevated marker levels return to normal post-operatively if no metastasis
  - β-hCG positive in 7% of pure seminomas, AFP never elevated with seminoma

Testes and scrotum have different lymphatic drainage, therefore trans-scrotal approach for biopsy or orchiectomy should be avoided

- testicular U/S (hypoechoic area within tunica albuginea = high suspicion of testicular cancer)
- evidence of testicular microlithiasis is not a risk factor for testicular cancer
- needle aspiration contraindicated

Staging
- clinical: CXR (lung mets), markers for staging (β-hCG, AFP, LDH), CT abdomen/pelvis (retroperitoneal lymphadenopathy)
  - Stage I: disease limited to testis, epididymis, or spermatic cord
  - Stage II: disease limited to the retroperitoneal nodes
  - Stage III: disease metastatic to supradiaphragmatic nodal or visceral sites

Table 22. 2010 TNM Classification of Testicular Carcinoma

T	N	M
Tis: intratubular germ cell neoplasia	**N0**: no regional lymph node metastasis	**M0**: no distant mets
T1: limited to testis and epididymis without vascular/lymphatic invasion	**N1**: Metastasis with a lymph node mass 2 cm or less in greatest dimension; or multiple lymph nodes, none more than 2 cm in greatest dimension	**M1**: distant mets **M1a**: nonregional lymph node(s) or pulmonary mets
T2: limited to testis and epididymis with vascular/lymphatic invasion	**N2**: Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension	**M1b**: distant mets other than to regional lymph nodes and lung
T3: invasion of the spermatic cord ± vascular/lymphatics	**N3**: Metastasis with a lymph node mass more than 5 cm in greatest dimension	
T4: invasion of the scrotum ± vascular/lymphatics		

Management
- orchiectomy through inguinal ligament for all stages
- consider sperm banking, testicular prosthesis
- adjuvant therapies (see figure 13)

Prognosis
- 99% cured with stage I and II disease
- 70-80% complete remission with advanced disease

Orchiopexy
Surgical descent (orchiopexy) of undescended testis does not eliminate the risk of malignancy, but allows for earlier detection by self-examination and reduces the risk of infertility

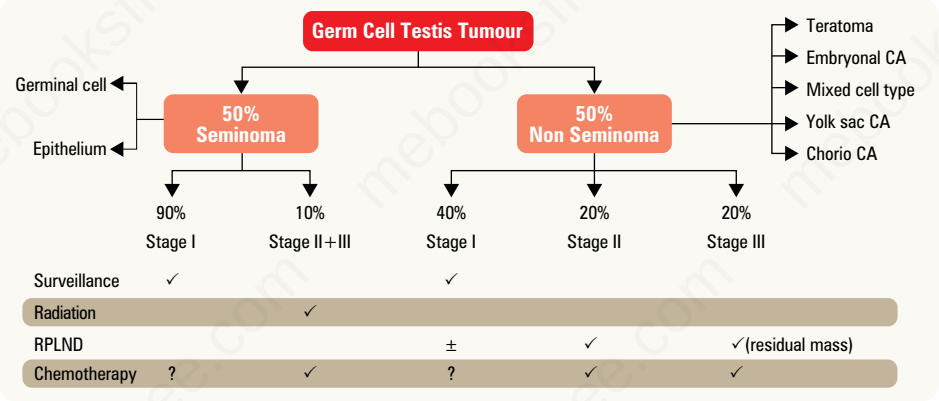


Figure 13. Adjuvant management of testicular cancer post-orchiectomy Adapted from Dr. MAS Jewett

Penile Tumours

Epidemiology
- rare (<1% of cancer in males in U.S.)
- most common in 6th decade

Benign
- cyst, hemangioma, nevus, papilloma

Pre-Malignant
- balanitis xerotica obliterans, leukoplakia, Buschke-Lowenstein tumour (large condyloma)

Pre-invasive Cancer
- carcinoma *in situ*
  - Bowen's disease → crusted, red plaques on the shaft
  - erythroplasia of Queyrat → velvet red, ulcerated plaques on the glans
  - treatment options: local excision, laser, radiation, topical 5-fluorouracil

Malignant
- risk factors
  - chronic inflammatory disease
  - STI
  - phimosis
  - uncircumcised penis
- 2% of all urogenital cancers
- SCC (>95%), basal cell, melanoma, Paget's disease of the penis (extremely rare)
- definitive diagnosis requires full thickness biopsy of lesion
- lymphatic spread (superficial/deep inguinal nodes → iliac nodes) >> hematogenous

Treatment
- wide surgical excision with tumour-free margins (dependent on extent and area of penile involvement) ± lymphadenectomy
- consider less aggressive treatment modalities in CIS (cryotherapy, laser therapy, etc.) if available

Scrotal Masses

Table 23. Differentiating between Scrotal Masses

Condition	Pain	Palpation	Additional Findings
Torsion	+	Diffuse tenderness Horizontal lie of testicle	Absent cremaster reflex, negative Prehn's sign
Epididymitis (U16)	+	Epididymal tenderness	Present cremaster reflex, positive Prehn's sign
Orchitis (U16)	+	Diffuse tenderness	Present cremaster reflex, positive Prehn's sign
Hematocele	+	Diffuse tenderness	No transillumination
Hydrocele	–	Testis not separable from hydrocele, cord palpable	Transillumination, Hx of trauma
Spermatocele	–	Testis separable from spermatocele, cord palpable	Transillumination
Varicocele	–	Bag of worms	No transillumination, increases in size with valsalva, decrease in size if supine
Indirect Inguinal	– (+ if strangulated)	Testis separable from hernia, cord not palpable, cough impulse may transmit, may be reducible	No transillumination
Tumour	– (+ if hemorrhagic)	Hard lump/nodule	
Generalized/ Dependent edema	–	Diffuse swelling	Often post-operative or immobilized, check for liver dysfunction
Idiopathic	–		

Varicocele Grading
- Grade 1: Palpable only with Valsalva manoeuvre
- Grade 2: Palpable without Valsalva
- Grade 3: Visible through scrotal skin

Suspect a Retroperitoneal Mass/Process in a Patient with a Varicocele if
- Acute onset
- Right sided (isolated)
- Palpable abdominal mass
- Does not reduce while supine

Indications for Treatment of Varicocele
- Impaired sperm quality or quantity
- Pain or dull ache affecting QOL
- Affected testis fails to grow in adolescents
- Cosmetic indications (especially in adolescents)

Table 24. Benign Scrotal Masses

Type	Varicocele	Spermatocele	Hydrocele	Testicular Torsion	Inguinal Hernia
Definition	Dilatation and tortuosity of pampiniform plexus	A benign, sperm filled epididymal retention cyst	Collection of serous fluid that results from a defect or irritation in the tunica vaginalis	Twisting of the testicle causing venous occlusion and engorgement as well as arterial ischemia and infarction	Protrusion of abdominal contents through the inguinal canal into the scrotum
Etiology	15% of men Due to incompetent valves in the testicular veins 90% left sided	Multiple theories, including: Distal obstruction Aneurysmal dilations of the epididymis Agglutinated germ cells	Usually idiopathic Found in 5-10% testicular tumours Associated with trauma/infection Communicating: patent processus vaginalis, changes size during day (peds) Non-communicating: non-patent processus vaginalis (adult)	Trauma Cryptorchidism "Bell clapper deformity" Many occur in sleep (50%) Necrosis of glands in 5-6 h	Indirect (through internal ring, often into scrotum): congenital Direct (through external ring, rarely into scrotum): abdominal muscle weakness
Hx/P/E	"Bag of worms" Often painless Pulsates with Valsalva	Non-tender, cystic mass Transilluminates	Non-tender, intrascrotal mass Cystic Transilluminates	Acute onset severe scrotal pain, swelling GI upsets cases Retracted and transverse testicle (horizontal lie) Negative Phren's sign Absent cremasteric reflex	A small bulge in the groin that may increase in size with Valsalva and disappear when lying down Can present as a swollen or enlarged scrotum Discomfort or sharp pain – especially when straining, lifting, or exercising
Investigations	P/E Valsava	P/E U/S to rule out tumour	U/S to rule out tumour	U/S Doppler with probe over testicular artery Decrease uptake on ^{99m}Tc-pertechnetate scintillation scan (doughnut sign)	Hx and P/E Invagination of the scrotum Valsalva
Treatment	Conservative Surgical ligation of testicular veins Percutaneous vein occlusion (balloon, sclerosing agents) Repair may improve sperm count/motility 50-75%	Conservative Avoid needle aspiration as it can lead to infection, reaccumulation and spilling of irritating sperm within scrotum Excise if symptomatic	Conservative Needle drainage Surgical	Emergency surgical exploration and bilateral orchiopexy Definitive diagnosis NOT necessary to take to OR Orchiectomy if poor prognosis	Surgical repair

TORSION OF TESTICULAR APPENDIX
- twisting of testicular/epididymal vestigial appendix

Signs and Symptoms
- clinically similar to testicular torsion, but vertical lie and cremaster reflex preserved
- "blue dot sign"
  - blue infarcted appendage seen through scrotal skin in children (can usually be palpated as small, tender lump)

Treatment
- analgesia – most will subside over 5-7 d
- surgical exploration and excision if refractory pain

HEMATOCELE
- trauma with bleed into tunica vaginalis
- U/S helpful to exclude fracture of testis which requires surgical repair

Treatment
- ice packs, analgesics, surgical repair

Acute scrotal swelling/pain in young boys is torsion until proven otherwise

Transillumination refers to light being transmitted through tissue (i.e. due to excess fluid)

Differential of a Benign Scrotal Mass

HIS BITS
Hydrocele
Infection (epididymitis/orchitis)
Sperm (spermatocele)
Blood (hematocele)
Intestines (hernia)
Torsion
Some veins (varicocele)

Penile Complaints

Table 25. Penile Complaints

Type	Peyronie's Disease (Figure 14)	Priapism	Paraphimosis	Phimosis	Premature Ejaculation
Definition	Acquired curvature of penile shaft secondary to fibrous thickening of tunica albuginea	Prolonged erection lasting >4 h in the absence of sexual excitement/ desire	Retracted Foreskin (behind glans penis) that cannot be reduced	Inability to retract foreskin over glans penis	Ejaculation prior to when one or both partners desire it, either before or soon after penetration
Etiology	Etiology unknown Trauma/repeated inflammation Familial predisposition Associated with DM, vascular disease, autoimmunity, Dupuytren's contracture, erectile dysfunction, urethral instrumentation	50% idiopathic **Ischemic (common)** Thromboembolic (sickle cell) **Non-Ischemic** Trauma Medications Neurogenic	Iatrogenic (post cleaning/ instrumentation) Trauma Infectious (balanitis, balanoposthitis)	Congenital (90% natural separation by age 3) Balanitis Poor Hygiene	Psychological factors Primary: no period of acceptable control Secondary: symptoms after a period of control, not associated with general medical condition
Hx/P/E	Penile curvature/shortening Pain with erection Poor erection distal to plaque	Painful erection ± signs of necrosis Note: *non-ischemic (high flow)* priapism may present without pain	Painful, swollen glans penis, foreskin Constricting band proximal to corona Dysuria, decreased urinary stream in children	Limitation and pain when attempting to retract foreskin Balanoposthitis (infection of prepuce)	Ejaculatory latency ≥1 min Inability to control or delay ejaculation Psychological distress
Investigations	Hx and P/E	Hx and P/E Cavernosal blood gas analysis Doppler US of the penis	Hx and P/E	Hx and P/E	Hx and P/E Testosterone levels if in conjunction with impotence
Treatment	Watchful waiting (spontaneous resolution in up to 12%) Medical management: Intralesional or topical verapamil Surgical management: Incision/ excision of plaque Shortening of less affected side ± penile prosthesis	Treat reversible causes **High-flow:** Self-limited Consider arterial embolization **Low-flow:** Needle aspirated decompression Phenylephrine intracorporeal injection q3-5min Surgical shunt no response within 1 h	Manual pressure (with analgesia) Dorsal slit Circumcision (urgent or electively to prevent recurrence)	Proper hygiene Topical corticiosterioids Dorsal slit Circumcision	Rule out medical condition Address psychiatric concerns, counselling **Medication:** SSRI or clomipramine Topical lidocaine-prilocaine

Erectile Dysfunction

Definition
- consistent (>3 mo duration) or recurrent inability to obtain or maintain an adequate erection for satisfactory sexual performance

Testosterone deficiency is an uncommon cause of ED

Physiology
- erection involves the coordination of psychologic, neurologic, hemodynamic, mechanical, and endocrine components
- nerves: sympathetic (T11-L2), parasympathetic (S2-4), somatic (dorsal penile/pudendal nerves [S2-4])
- erection ("POINT")
  - parasympathetics → NO release → increased cGMP within corpora cavernosa leading to:
    1. arteriolar dilatation
    2. sinusoidal smooth muscle relaxation → increased arterial inflow and compression of penile venous drainage (decreased venous outflow)

Erections POINT AND SHOOT
parasympathetics = **point**; and **s**ympathetics/ **s**omatics = **shoot**

- emission ("SHOOT")
  - sensory afferents from glans
  - secretions from prostate, seminal vesicles, and ejaculatory ducts enter prostatic urethra (sympathetics)
- ejaculation ("SHOOT")
  - bladder neck closure (sympathetic)
  - spasmodic contraction of bulbo-cavernosus and pelvic floor musculature (somatic)
- detumescence
  - sympathetic nerves, norepinephrine, endothelin-1 → arteriolar and sinusoidal constriction → penile flaccidity

Classification

Table 26. Classification of Erectile Dysfunction

	Psychogenic*	Organic*
Proportion	10%	90%
Onset	Sudden	Gradual
Frequency	Sporadic	All circumstances
Variation	With partner and circumstance	No
Age	Younger	Older
Organic Risk Factors (HTN, DM, dyslipidemia)	No organic risk factors	Risk factors present
Nocturnal/AM Erection	Present	Absent

*Combination can co-exist

Etiology ("IMPOTENCE")

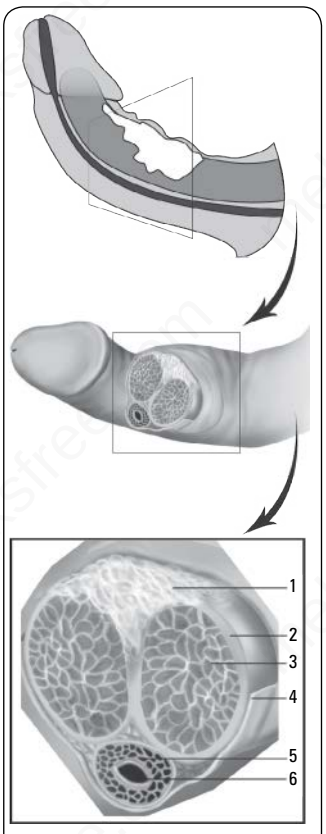
- **I**atrogenic: pelvic surgery, pelvic radiation
- **M**echanical: Peyronie's, post-priapism
- **P**sychological: depression, stress, anxiety, PTSD, widower syndrome
- **O**cclusive: arterial HTN, DM, smoking, hyperlipidemia, PVD, impaired veno-occlusion
- **T**rauma: penile/pelvic, bicycling
- **E**xtra factors: renal failure, cirrhosis, COPD, sleep apnea, malnutrition
- **N**eurogenic: CNS (e.g. Parkinson's, MS, spinal cord injury, Guillain-Barré, spina bifida, stroke), PNS (e.g. DM, peripheral neuropathy)
- **C**hemical: antihypertensives, sedatives, antidepressants, antipsychotics, anxiolytics, anticholingerics, antihistamines, anti-androgens (including 5-α reductase inhibitors), statins, GnRH agonists, illicit drugs
- **E**ndocrine: DM, hypogonadism, hyperprolactinemia, hypo/hyperthyroid

Diagnosis

- complete Hx (include sexual, medical, and psychosocial aspects)
- self-administered questionnaires (e.g. International Index of Erectile Function, Sexual Health Inventory for Men Questionnaire, ED Intensity Scale, ED Impact Scale)
- focused P/E, including vascular and neurologic examinations, secondary sexual characteristics
- lab investigations, dependent on clinical picture
  - risk factor evaluation: fasting blood glucose or HbA1c, cholesterol profile
  - optional: TSH, CBC, U/A, testosterone (free and total), prolactin, LH
- specialized testing including nocturnal penile tumescence monitoring usually unnecessary
- evaluation of penile vasculature only relevant with past history of trauma (i.e. pelvic fracture)

Treatment

- can often be managed by family doctor, see sidebar for when to refer
- must fully inform patient/partner of options, benefits and complications
- non-invasive
  - lifestyle changes (alcohol, smoking), psychological (sexual counselling and education)
  - change precipitating medications
  - treat underlying causes (DM, CVD, HTN, endocrinopathies)
- minimally invasive
  - oral medication (see *Common Medications*, U42)
    - sildenafil, tadalafil, vardenafil, avanafil (not available in Canada): inhibits PDE-5 to increase intracavernosal cyclic GMP levels
      - all four have similar effectiveness, difference in onset of action is not clinically significant
      - tadalafil has longer half-life, no cyanopsia, and can be taken on empty or full stomach
    - vacuum devices: draw blood into penis via negative pressure, then put ring at base of penis
    - MUSE: male urethral suppository for erection – vasoactive substance (PGE1) capsule inserted into urethra
- invasive
  - intracavernous vasodilator injection/self-injection
    - triple therapy (papaverine, phentolamine, PGE1) or PGE1 alone
    - complications: priapism (overdose), fibrosis of tunica albuginea at site of repeated injections (Peyronie's plaque) and injection site injuries (pain, hematoma, etc.)
- surgical
  - penile implant (last resort): malleable or inflatable
  - penile artery reconstruction (in young men with isolated vascular lesion – investigational)



1. Fibrous plaque
2. Tunica albuginea
3. Corpus cavernosum
4. Buck's fascia
5. Corpus spongiosum
6. Urethra

© June Li

Figure 14. Peyronie's disease

Penile vascular abnormalities may be a marker of risk for CV disease. Young men with vascular ED have 50x higher risk of having a CV event

When to Consider Referral

FAT PEN
Failed medical therapy
penile **A**natomic abnormality
pelvic/perineal **T**rauma
Psychogenic cause
Endocrinopathy
vascular/**N**eurologic assessment

PDE-5 inhibitors are contraindicated in patients on nitrates/nitroglycerin due to severe hypotension

Initial trial of MUSE® or intracavernosal injection should be done under medical supervision

Trauma

• see Emergency Medicine, ER7

Renal Trauma

Classification According to Severity
- minor
  - contusions and superficial lacerations/hematomas: 90% of all blunt traumas, surgical exploration seldom necessary
- major
  - laceration that extends into medulla and collecting system, major renal vascular injury, shattered kidney

Etiology
- 80% blunt (MVC, assaults, falls) vs. 20% penetrating (stab wounds and gunshots)

Clinical Features
- mechanism of injury raises suspicion
- can be hemodynamically unstable secondary to renal vascular injury and/or other sustained injuries: ABCs
- upper abdominal tenderness, flank tenderness, flank contusions, lower rib/vertebral transverse process fracture

Investigations
- U/A
  - hematuria: requires workup but degree does not correlate with the severity of injury
- imaging
  - CT (contrast, triphasic) if patient stable: look for renal laceration, extravasation of contrast, retroperitoneal hematoma, and associated intra-abdominal organ injury

Staging (does not necessarily correlate well with clinical status)
- I: contusion/hematoma
- II: <1 cm laceration without urinary extravasation
- III: >1 cm laceration without urinary extravasation
- IV: laceration causing urinary extravasation and/or main arterial or vein injury with contained hematoma
- V: shattered kidney or avulsion of pedicle

Treatment
- microscopic hematuria + isolated well-staged minor injuries → no hospitalization
- gross hematuria + contusion/minor lacerations → hospitalize, bedrest, repeat CT if bleeding persists
- surgical intervention/minimally invasive angiography and embolization
  - absolute indications
    - hemorrhage and hemodynamic instability
  - relative indications
    - non-viable tissue and major laceration
    - urinary extravasation
    - vascular injury
    - expanding or pulsating peri-renal mass
    - laparotomy for associated injury
- follow-up with U/S or CT before discharge, and at 6 wk

Complications
- HTN in 5% of renal trauma

Bladder Trauma

Classification
- contusions: no urinary extravasation, damage to mucosa or muscularis
- intraperitoneal ruptures: often involve the bladder dome
- extraperitoneal ruptures: involve anterior or lateral bladder wall in full bladder

Etiology
- blunt (MVC, falls, and crush injury) vs. penetrating trauma to lower abdomen, pelvis, or perineum
- blunt trauma is associated with pelvic fracture in 97% of cases

Clinical Features
- abdominal tenderness, distention, peritonitis, and inability to void
- can be hemodynamically unstable secondary to pelvic fracture, other sustained injuries: ABCs
- suprapubic pain

Investigations
- U/A: gross hematuria in 90%
- imaging (including CT cystogram and post-drainage films for extravasation)

Treatment
- penetrating trauma → surgical exploration
- contusion → urethral catheter until hematuria completely resolves
- extraperitoneal bladder perforations → typically non-operative with foley insertion, and follow with cystograms
  - surgery if: infected urine, rectal/vaginal perforation, bony spike into bladder, laparotomy for concurrent injury, bladder neck involvement, persistent urine leak and failed conservative management
- intraperitoneal rupture usually requires surgical repair and suprapubic catheterization

Complications
- complications of bladder injury itself are rare
- mortality is around 20%, and is usually due to associated injuries rather than bladder rupture

Urethral Injuries

Etiology
- posterior urethra
  - common site of injury is junction of membranous and prostatic urethra due to blunt trauma, MVCs, pelvic fracture
  - shearing force on fixed membranous and mobile prostatic urethra
- anterior urethra
  - straddle injury can crush bulbar urethra against pubic rami
- other causes
  - iatrogenic (instrumentation, prosthesis insertion), penile fracture, masturbation with urethral manipulation
- always look for associated bladder rupture

Clinical Features
- blood at urethral meatus
- high-riding prostate on DRE
- swelling and butterfly perineal hematoma
- penile and/or scrotal hematoma
- sensation of voiding without U/O
- distended bladder

All patients with suspected urethral injury should undergo RUG

Investigations
- must perform RUG or cystoscopy prior to catheterization

Treatment
- simple contusions
  - no treatment
- partial urethral disruption
  - very gentle attempt at catheterization by urologist
  - with no resistance to catheterization → Foley x 2-3 wk
  - with resistance to catheterization → suprapubic cystostomy or urethral catheter alignment
- periodic flow rates/urethrograms to evaluate for stricture formation
- complete disruption
  - immediate repair if patient stable, delayed repair if unstable (suprapubic tube in interim)

Complications
- stricture

Infertility

Definition
- failure to conceive after one year of frequent, unprotected and properly timed intercourse
- incidence
  - 15% of all couples (35-40% female, 20% male, 25-30% combined)

Female Factors

- see Gynecology, GY23

Male Factors

Male Reproduction
- hypothalamic-pituitary-testicular axis (HPTA)
  - pulsatile GnRH from hypothalamus acts on anterior pituitary stimulating release of LH and FSH
  - LH acts on Leydig (interstitial) cells → testosterone synthesis and secretion
  - FSH acts on Sertoli cells → structural and metabolic support to developing spermatogenic cells
  - FSH and testosterone support germ cells (responsible for spermatogenesis)
  - sperm route: epididymis → vas deferens → ejaculatory ducts → prostatic urethra

Etiology
- idiopathic (40-50% infertile males)
- testicular
  - varicocele (35-40% infertile males)
  - tumour
  - congenital (Klinefelter's triad: small, firm testes, gynecomastia, and azoospermia)
  - post-infectious (epididymo-orchitis, STIs, mumps)
  - uncorrected torsion
  - cryptorchidism (<5% of cases)
- obstructive
  - iatrogenic (surgery: see below)
  - infectious (gonorrhea, chlamydia)
  - trauma
  - congenital (absence of vas deferens, CF)
  - bilateral ejaculatory duct obstruction, epididymal obstructions
  - Kartagener's syndrome (autosomal recessive disorder causing defect in action of cilia)
- endocrine (see Endocrinology, E45)
- HPTA (2-3%) e.g. Kallmann's syndrome (congenital hypothalamic hypogonadism), excess prolactin, excess androgens, excess estrogens
- other
  - retrograde ejaculation secondary to surgery
  - medications
  - prior exposure to chemotherapy or pelvic radiation
  - drugs: marijuana, cocaine, tobacco, alcohol
  - increased testicular temperature (sauna, hot baths, tight pants or underwear)
  - chronic disease: e.g. liver, renal

History
- age of both partners
- medical: past illness, DM, trauma, CF, genetic syndromes, STIs, cryptorchidism
- surgical: vasectomy, herniorrhaphy, orchidopexy, prostate surgery
- fertility: pubertal onset, previous pregnancies, duration of infertility, treatments
- sexual: libido, erection/ejaculation, timing, frequency
- family Hx
- medications: cytotoxic agents, GnRH agonists, anabolic steroids, nitrofurantoin, cimetidine, sulfasalazine, spironolactone, α-blockers
- social Hx: alcohol, tobacco, cocaine, marijuana, school performance/learning disabilities (suggestive of Klinefelter syndrome)
- occupational exposures: radiation, heavy metals

Physical Exam
- general appearance: sexual development, gynecomastia, obesity, pubic hair
- scrotal exam: size, consistency, and nodularity of testicles; palpation of cord for presence of vas deferens; DRE; valsalva for varicocele

Investigations

- semen analysis (SA) at least 2 specimens, collected 1-2 wk apart
- hormonal evaluation
  - indicated with abnormal SA (rare to be abnormal with normal SA)
  - testosterone and FSH
  - serum LH and prolactin are measured if testosterone or FSH are abnormal
- genetic evaluation
  - chromosomal studies (Klinefelter's syndrome – XXY)
  - genetic studies (Y-chromosome microdeletion, CF gene mutation)
- immunologic studies (antisperm antibodies in ejaculate and blood)
- testicular biopsy
- scrotal U/S (varicocele, testicular size)
- vasography (assess patency of vas deferens)

Treatment

- assessment of partner
- lifestyle
  - regular exercise, healthy diet
  - eliminate alcohol, tobacco and illicit drugs
- medical
  - endocrine therapy (see Endocrinology, E)
  - treat retrograde ejaculation
  - discontinue anti-sympathomimetic agents, may start α-adrenergic stimulation (phenylpropanolamine, pseudoephedrine, or ephedrine)
  - treat underlying infections
- surgical
  - varicocelectomy (if indicated)
  - vasovasostomy (vasectomy reversal) or epididymovasostomy
  - transurethral resection of blocked ejaculatory ducts
- assisted reproductive technologies (ART)
  - refer to infertility specialist
  - sperm washing + intrauterine insemination (IUI)
  - *in vitro* fertilization (IVF)
  - intracytoplasmic sperm injection (ICSI) after CF screening of patient and partner in patients with congenital bilateral absence of vas deferens

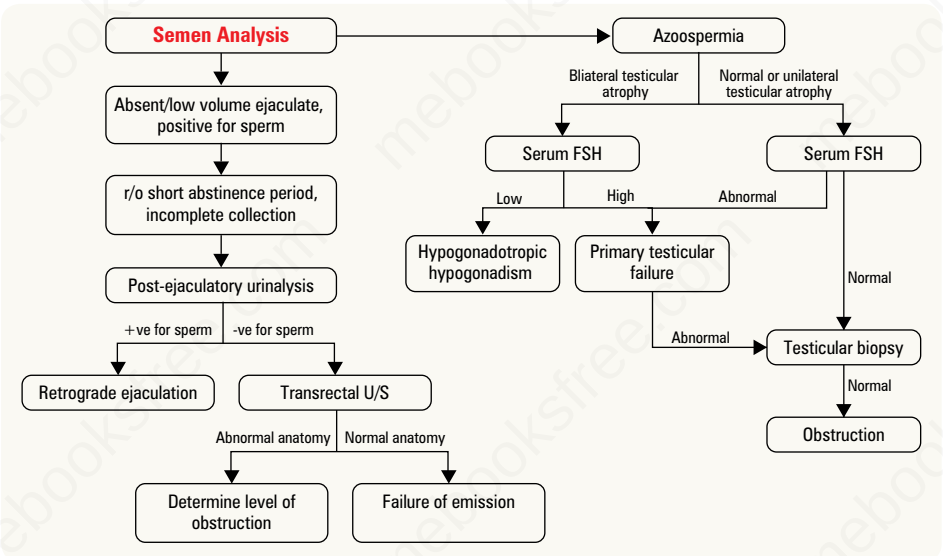


Figure 15. Infertility workup

Normal Semen Values
- Volume: 2-5 mL
- Concentration: >15 million sperm/mL
- Morphology: 30% normal forms
- Motility: >40% adequate forward progression
- Liquefaction: complete in 20 min
- pH: 7.2-7.8
- WBC: <10/HPF or <106 WBC/mL semen

Common Terminology on SA
- Teratospermia: Abnormal morphology
- Asthenospermia: Abnormal motility
- Oligospermia: Decreased sperm count
- Azoospermia: Absent sperm in semen
- Mixed types: i.e. oligoasthenospermia

Mutation of cystic fibrosis transmembrane conductance regulator (CFTR) gene is associated with congenital bilateral absence of vas deferens and epididymal cysts, even if patient manifests no symptoms of CF

WHO Guidelines
Male Infertility Factors

SPERM COUNT
Systemic factor/Smoking
Psychological illness
Endocrinopathy
Retrograde ejaculation
Medications
Chronic disease
Obstructive
Unexplained
Narcotics
Testicular

Pediatric Urology

Congenital Abnormalities

- not uncommon; 1/200 have congenital abnormalities of the GU tract
- six common presentations of congenital urological abnormalities

1. ANTENATAL HYDRONEPHROSIS

Majority of antenatal hydronephroses resolve during pregnancy or within the first year of life

Epidemiology
- 1-5% fetal U/S, some detectable as early as first trimester
- most common urological consultation in perinatal period and one of most common U/S abnormalities of pregnancy

Differential Diagnosis
- UPJ or UVJ obstruction
- multi-cystic dysplastic kidney
- VUR
- PUVs (only in boys)
- duplication anomalies
- ureterocele
- ectopic ureter

Treatment
- antenatal *in utero* intervention rarely indicated unless evidence of lower urinary tract obstruction with oligohydramnios

2. POSTERIOR URETHRAL VALVES

Epidemiology
- the most common congenital obstructive urethral lesion in male infants

Pathophysiology
- abnormal mucosal folds at the distal prostatic urethra causing varying degrees of obstruction

Clinical Presentation
- dependent on age
  - antenatal: bilateral hydronephrosis, distended bladder, oligohydramnios
  - neonatal (recognized at birth): palpable abdominal mass (distended bladder, hydronephrosis), urinary ascites (transudation of retroperitoneal urine), respiratory distress (pulmonary hypoplasia from oligohydramnios), weak urinary stream
  - neonatal (not recognized at birth): within weeks present with urosepsis, dehydration, electrolyte abnormalities, failure to thrive; rule out pyloric stenosis, which may present similarly
  - toddlers: UTIs or voiding dysfunction
  - school-aged boys: voiding dysfunction → urinary incontinence
- associated findings include renal dysplasia and secondary VUR

Investigations
- most commonly recognized on prenatal U/S → bilateral hydronephrosis, thickened bladder, dilated posterior urethra ("keyhole sign"), oligohydramnios in a male fetus
- VCUG → dilated and elongated posterior urethra, trabeculated bladder, VUR

Treatment
- immediate catheterization to relieve obstruction, followed by cystoscopic resection of PUV when baby is stable
- if resection of PUV is not possible, vesicostomy is indicated

3. URETEROPELVIC JUNCTION OBSTRUCTION

Etiology
- unclear: adynamic ureteral segment, stenosis, strictures, extrinsic compression, aberrant blood vessels
- can rarely be secondary to tumour, stone, etc, in children

Epidemiology
- the most common congenital defect of the ureter
- M:F = 2:1
- up to 40% bilateral, which may be associated with worse prognosis

Clinical Presentation
- symptoms depend on severity and age at diagnosis (mostly asymptomatic finding on antenatal U/S)
  - infants: abdominal mass, urinary infection
  - children: pain, vomiting, failure to thrive
- some cases are diagnosed after puberty and into adulthood
  - in adolescents and adults, the symptoms may be triggered by episodes of increased diuresis, such as following alcohol ingestion (Dietl's crisis)

Investigations
- antenatal: serial U/S most common, and renal scan ± furosemide

Treatment
- surgical correction (pyeloplasty), consider nephrectomy if <15% differential renal function

4. VESICOURETERAL REFLUX

Definition
- retrograde passage of urine from the bladder, through the UVJ, into the ureter

Classification
- primary reflux: incompetent or inadequate closure of UVJ
  - lateral ureteral insertion, short submucosal segment
- secondary reflux: abnormally high intravesical pressure resulting in failure of UVJ closure
  - often associated with anatomic (PUV) or functional (neuropathic) bladder dysfunction

Epidemiology
- estimated ~1% of newborns, but not well known
- incidence and clinical relevance higher in children with febrile UTIs and prenatal hydronephrosis
- risk factors: race (white > black), female gender, age (<2 yr), genetic predisposition

Investigations
- focused Hx, particularly of voiding dysfunction (frequency, urgency, diurnal enuresis, constipation, encopresis)
  - also screen for infections (UTI, pyelonephritis, urosepsis) and renal failure (uremia, HTN)
- initial evaluation of renal status, growth parameters, and blood pressure is warranted in any child with VUR due to relatively high incidence of renal scarring
  - height, weight, blood pressure
  - serum Cr
  - U/A, C&S
  - renal U/S
  - DMSA renal scan if at high risk (greater sensitivity in detecting structural defects associated with dysplasia, renal scarring or pyelonephritis; entails radiation exposure)
  - sibling family screening is controversial

Treatment
- spontaneous resolution in 60% of primary reflux
  - in lower grades (I-III), goal is to prevent infection or renal damage via medical treatment
- medical treatment: daily ABx prophylaxis at half the treatment dose for acute infection (see Table 9, U12 - TMP/SMX, trimethoprim, amoxicillin, or nitrofurantoin)
- surgical treatment: ureteral reimplantation ± ureteroplasty, or subureteral injection with bulking agents (Deflux® or Macroplastique®)
  - indications include failure of medical management, renal scarring (e.g. renal insufficiency, HTN), breakthrough UTIs, persistent high grade (IV or V) reflux

5. HYPOSPADIAS

Definition
- a condition in which the urethral meatus opens on the ventral side of the penis, proximal to the normal location in the glans penis
- depending on severity, may result in difficulty directing urinary stream, having intercourse or depositing sperm in vagina

Epidemiology
- very common; 1/300 live male births
- distal hypospadias more common than proximal
- white >> black
- may be associated with ventral penile curvature, disorders of sexual differentiation, undescended testicles or inguinal hernia

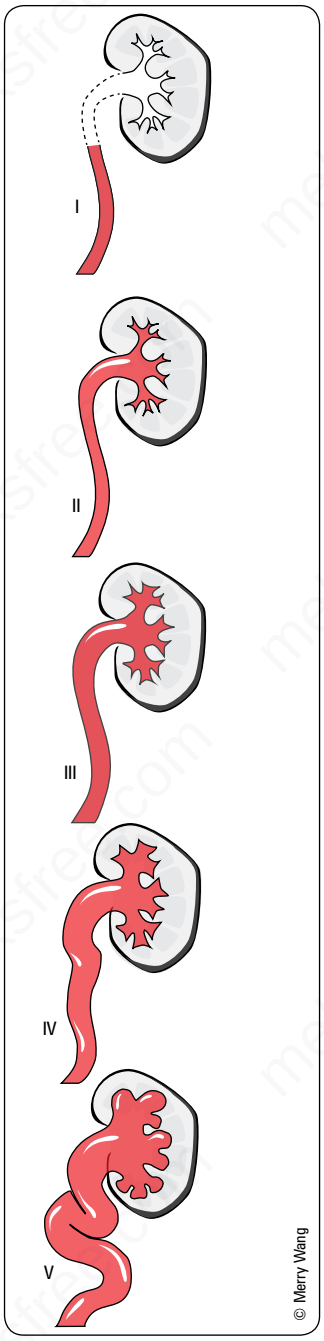


Figure 16. VUR grading (based on cystogram)

VUR Grading (based on cystogram)
- Grade I: ureters only fill
- Grade II: ureters and pelvis fill
- Grade III: ureters and pelvis fill with some dilatation
- Grade IV: ureters, pelvis, and calyces fill with significant dilatation
- Grade V: ureters, pelvis, and calyces fill with major dilatation and tortuosity

Defer circumcision in patients with hypospadias

Treatment
- early surgical correction; optimal repair before 2 yr
- neonatal circumcision should be deferred because the foreskin may be utilized in the correction

6. EXSTROPHY-EPISPADIAS COMPLEX

Definition
- a spectrum of defects depending on the timing of the rupture of the cloacal membrane
  - bladder exstrophy: congenital defect of a portion of lower abdominal and anterior bladder wall, with exposure of the bladder lumen
  - cloacal exstrophy
    - exposed bladder and bowel with imperforate anus
    - associated with spina bifida in >50%
  - epispadias (least severe)
    - urethra opens on dorsal aspect of the penis, often associated with penile curvature

Etiology
- represents failure of closure of the cloacal membrane, resulting in the bladder and urethra opening directly through the abdominal wall

Epidemiology
- rare: incidence 1/30,000, M:F = 3:1 predominance
- high morbidity → multiple reconstructive surgeries, incontinence, infertility, reflux

Treatment
- surgical correction at birth
- later corrections for incontinence, VUR, and low bladder capacity may be needed

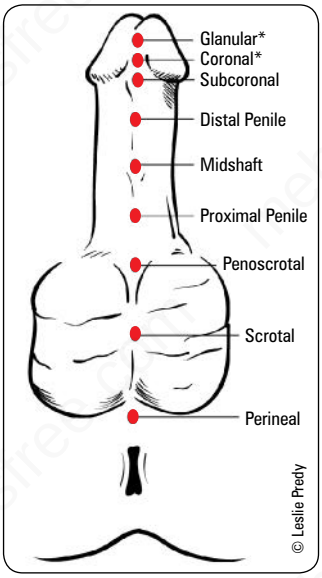


Figure 17. Classification of hypospadias
(*account for 75%)

Nephroblastoma (Wilms' Tumour)

Etiology
- arises from abnormal proliferation of metanephric blastema

Epidemiology
- 5-5-10: 5% of all childhood cancers, 5% bilateral, 10% associated with congenital malformation syndromes
- most common primary malignant renal tumour of childhood
- average age of incidence is 3 yr

Clinical Features
- abdominal mass: large, firm, unilateral (80%)
- HTN (25%)
- flank tenderness (30-40%)
- microscopic hematuria (12-25%)
- nausea/vomiting

Treatment
- always investigate contralateral kidney and renal vein (for tumour thrombus)
- unilateral disease: radical nephrectomy ± radiation ± chemotherapy
- bilateral disease: nephron-sparing surgery following neoadjuvant chemotherapy

Prognosis
- 5 yr survival 80%

Cryptorchidism/Ectopic Testes

Definition
- abnormal location of testes somewhere along the normal path of descent (external inguinal ring > inguinal canal > abdominal)
- Denis Browne pouch (between external oblique fascia and Scarpa's fascia) most common
- differential diagnosis:
  - retractile testes
  - atrophic testes
  - disorders of sexual differentiation (bilateral impalpable gonads)

Epidemiology
- 2.7% of full term newborns
- 0.7-0.8% at 1 yr

Normal Testicular Development and Descent in Utero
2nd month: Testicle begins to form
4th month: Begins to take on its normal appearance and migrates from its origin at the kidney to the internal inguinal ring
7th month: The testis, surrounded in peritoneal covering, begins to descend through the internal ring, inguinal canal and external ring to terminate in the scrotum

Treatment
- orchiopexy
- hormonal therapy not proven to be of benefit over standard surgical treatment

Prognosis
- reduction in fertility
  - untreated bilateral cryptorchidism: ~100% infertility
  - paternity rates: 53%, 90%, and 93% in formerly bilateral cryptorchid, formerly unilateral cryptorchid, and normal men, respectively
- increased malignancy risk
  - intraabdominal > inguinal
  - surgical correction facilitates testicular monitoring and may reduce malignancy risk
- increased risk of testicular torsion (reduced by surgical correction)

Disorders of Sexual Differentiation

Definition
- formerly known as intersex disorders: considered social emergency
- abnormal genitalia for chromosomal sex due to the undermasculinization of males or the virilization of females

Classification
1. 46 XY DSD
   - defect in testicular synthesis of androgens
   - androgen resistance in target tissues
   - palpable gonad
2. 46 XX DSD
   - most due to CAH (21-hydroxylase deficiency most common enzymatic defect) → shunt in steroid biosynthetic pathway leading to excess androgens
   - undiagnosed and untreated CAH can be associated with life-threatening electrolyte abnormalities in the newborn (salt-wasting CAH)
3. ovotesticular DSD
4. mixed gonadal dysgenesis (46 XY/45 XO most common karyotype)
   - presence of Y chromosome → partial testis determination to varying degrees

A phenotypic male newborn with bilateral non-palpable testicles should be considered 46XX with salt-wasting CAH and must undergo proper evaluation prior to discharge

Diagnosis
- thorough family Hx noting any consanguinity
- maternal Hx, especially medication/drug use during pregnancy (maternal hyperandrogenemia)
- P/E: palpable gonad (= chromosomal male), hyperpigmentation, evidence of dehydration, HTN, stretched phallus length, position of urethral meatus
- laboratory tests
  - plasma 17-OH-progesterone (after 36 h of life) → increased in CAH
  - plasma 11-deoxycortisol → increased in 11-β-hydroxylase deficiency
  - basal adrenal steroid levels
  - serum testosterone and DHT pre- and post-hCG stimulation (2,000 IU/d for 4 d)
  - serum electrolytes
  - chromosomal evaluation including sex karyotype
- U/S of adrenals, gonads, uterus, and fallopian tubes
- endoscopy and genitography of urogenital sinus

Treatment
- steroid supplementation as indicated (e.g. CAH)
- sex assignment after extensive family consultation
  - must consider capacity for sexually functioning genitalia in adulthood, fertility potential, and psychological impact
- reconstruction of external genitalia between 6 and 12 mo
- long-term psychological guidance and support for both patient and family

Enuresis

- see Pediatrics, P9

Selected Urological Procedures

Bladder Catheterization

- catheter size measured by the French (Fr) scale – circumference in mm
- each 1 mm increase in diameter = approximately 3 Fr increase (standard size 14-18 Fr)
- should be removed as soon as possible to reduce the risk of UTI

Continuous Catheterization

- indications
  - accurate monitoring of U/O
  - relief of urinary retention due to medication, neurogenic bladder, or intravesical obstruction
  - temporary therapy for urinary incontinence
  - perineal wounds
  - clot prevention (22-24 Fr) for CBI
  - intra- and post-operative
  - comfort for end of life care

Alternatives to Continuous Catheterization

- intermittent catheterization
  - PVR measurement
  - to obtain sterile diagnostic specimens for U/A, urine C&S
  - management of neurogenic bladder or chronic urinary retention
- condom catheter
- suprapubic catheter

Causes of Difficult Catheterizations and Treatment

- patient discomfort → use sufficient lubrication (± xylocaine)
- collapsing catheter → lubrication as above ± firmer or larger catheter (silastic catheter)
- meatal/urethral stricture → dilate with progressively larger catheters/balloon catheter
- BPH → use coudé catheter as angled tip can help navigate around enlarged prostate
- urethral disruption/obstruction → filiform and followers or suprapubic catheterization
- anxious patient → anxiolytic medication

Complications of Catheterization

- infection: UTI, bladder fistula, bladder perforation (rare)
- meatal/urethral trauma

Contraindications

- trauma: blood at the urinary meatus, scrotal hematoma, pelvic fracture, and/or high riding prostate

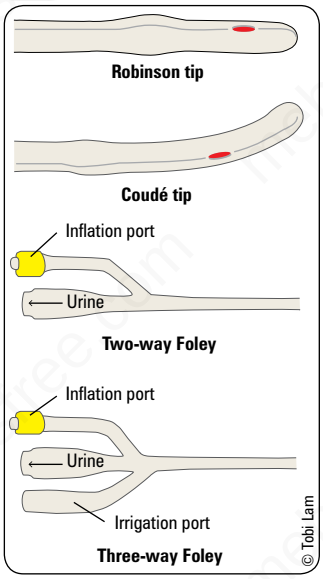


Figure 18. Transurethral (Foley) catheters

Male Circumcision for Prevention of Heterosexual Acquisition of HIV in Men
Cochrane DB Syst Rev 2009;2:CD003362
Purpose: To evaluate the effectiveness and safety of male circumcision for preventing acquisition of HIV in heterosexual men.
Methods: The analyzed data is from three randomized controlled trials to assess the efficacy of male circumcision for preventing HIV acquisition in men in Africa.
Results: Medical male circumcision reduces the acquisition of HIV by heterosexual men (38-66% over 24 mo).

Circumcision Status and Risk of HIV and Sexually Transmitted Infections among Men who have Sex with Men: A Meta-Analysis
JAMA 2008;300:1674-1684
Purpose: To describe the association between male circumcision and HIV infection and other sexually transmitted infections (STIs) among men who have sex with men (MSM).
Methods: Meta-analysis of 15 studies (n=53,567)
Results: The associations between circumcision and HIV-positive and STIs were not statistically significant. Male circumcision had a protective association with HIV in studies of MSM conducted before the introduction of highly active anti-retroviral therapy.
Conclusions: There is insufficient evidence to support that male circumcision protects against HIV infection or other STIs.

Circumcision

Definition

- removal of some or all of the foreskin from the penis

Epidemiology

- 30% worldwide
- frequency varies with geography, religious affiliation, socioeconomic status

Medical Indications

- phimosis and recurrent paraphimosis
- recurrent UTIs (particularly in infants and in association with other urinary abnormalities)
- balanitis xerotica obliterans or other chronic inflammatory conditions

Contraindications

- unstable or sick infant
- congenital genital abnormalities (hypospadias)
- family Hx of bleeding disorders warrants laboratory investigation prior to circumcision

Complications

- bleeding
- infection
- penile entrapment, skin bridges
- fistula
- glans injury
- penile sensation deficits

Male Circumcision
Pediatrics 2012;130:e756-e785
Study: Guidelines by the American Academy of Pediatrics (AAP).
Recommendations: The American Academy of Pediatrics radically changed their position on male circumcision in 2012. The report from the AAP now states that the preventative health benefits outweigh the risks of the procedure and that the procedure is well-tolerated with adequate pain management and sterility. Stated benefits include the prevention of urinary tract infection, penile cancer, transmission of some sexually transmitted infections, including HIV. There is believed to be no effect on penile sexual function, sensitivity or sexual satisfaction. Acute complications are rare and more common if the procedure is done by an untrained provider.
Note: The Canadian Pediatric Society (CPS) has not yet updated their position on male circumcision since 1996, which stated that the CPS is opposed to routine circumcision. A new statement is expected soon.

Cystoscopy

Objective
- endoscopic inspection of the lower urinary tract (urethra, prostate, bladder, and ureteral orifices), samples for cytology
- scopes can be flexible or rigid

Indications
- gross hematuria
- LUTS (storage or voiding)
- urethral and bladder neck strictures
- bladder stones
- bladder tumour surveillance
- evaluation of upper tracts with retrograde pyelography (ureteric stents, catheters)

Complications
- during procedure
  - bleeding
  - anesthetic-related
  - perforation (rare)
- post-procedure (short-term)
  - infections (antibiotic prophylaxis recommended)
  - urinary retention
- post-procedure (long-term)
  - stricture

Radical Prostatectomy

Objective
- the removal of the entire prostate and prostatic capsule via a lower midline abdominal incision, laparoscopically or robotically
  - internal iliac and obturator vessel lymph nodes may also be dissected and sent for pathology (dependent on risk: clinical stage, grade, PSA)
  - seminal vesicle vessels are also partially or completely removed

Indications
- treatment for localized prostate cancer

Complications
- immediate (intraoperative)
  - blood loss
  - rectal injury (extremely rare)
  - ureteral injury (extremely rare)
- perioperative
  - lymphocele formation if concurrent pelvic lymphadenectomy performed)
- late
  - moderate to severe urinary incontinence (3-10%)
  - mild urinary incontinence (20%)
  - ED (~50%, depending on whether one, both, or neither of the neurovascular bundles are involved in extracapsular extension of tumour)

Retropubic, Laparoscopic, and Robot-Assisted Radical Prostatectomy: A Critical Review of Outcomes Reported by High-Volume Centres
J Endourology 2010;24:2003-2015
Study: A systematic review to compare perioperative outcomes, positive surgical margin (PSM) rates, and functional outcomes in retropubic radical prostatectomy (RRP) laparoscopic RP (LRP) and robot-assisted radical prostatectomy (RARP).
Methods: Medline database was searched. Weighted means (based on number of participants in each study) were calculated for all outcomes.
Results: 58 articles were reviewed. LRP and RARP were associated with better perioperative outcomes compared to RRP. RRP, LRP, and RARP had similar post-operative complication rates ranging from 10.3-10.98%. RARP had a lower overall PSM rate than LRP, and RRP. RARP had the highest continence rate and mean potency rates.
Conclusion: In high-volume centres, RRP, LRP and RARP are safe options for treating patients with localized prostate cancer. LRP and RARP are associated with better perioperative outcomes and RARP showed lower PSM rates, higher potency and continence compared to RRP and LRP.

Transurethral Resection of the Prostate (TURP)

Objective
- to partially resect the periurethral portion of the prostate (transition zone) to decrease symptoms of urinary tract obstruction
- accomplished via a transurethral (cystoscopic) approach using an electrocautery loop, irrigation (glycine), and illumination

Indications
- obstructive uropathy (large bladder diverticula, renal insufficiency)
- refractory urinary retention
- recurrent UTIs
- recurrent gross hematuria
- bladder stones
- intolerance/failure of medical therapy

Complications
- acute
  - intra- or extraperitoneal rupture of the bladder
  - rectal perforation
  - incontinence
  - incision of the ureteral orifice (with subsequent reflux or ureteral stricture)
  - hemorrhage
  - epididymitis
  - sepsis
  - transurethral resection syndrome (also called "post-TURP syndrome")
    - caused by absorption of a large volume of the hypotonic irrigation solution used, usually through perforated venous sinusoids, leading to a hypervolemic hyponatremic state
    - characterized by dilutional hyponatremia, confusion, nausea, vomiting, HTN, bradycardia, visual disturbances, CHF, and pulmonary edema
    - treat with diuresis and (if severe) hypertonic saline administration
- chronic
  - retrograde ejaculation (>75%)
  - ED (5-10% risk increases with increasing use of cautery)
  - incontinence (<1%)
  - urethral stricture
  - bladder neck contracture

Extracorporeal Shock Wave Lithotripsy

Objective
- to treat renal and ureteral calculi (proximal, middle or distal) which cannot pass through the urinary tract naturally
- shockwaves focused onto stone → fragmentation, allowing stone fragments to pass spontaneously and less painfully

Indications
- potential first-line therapy for renal and ureteral calculi <2.5 cm
- individuals with calculi in solitary kidney
- individuals with HTN, DM or renal insufficiency

*patient preference and wait-times play a large role in stone management

Contraindications
- acute UTI or urosepsis
- bleeding disorder or coagulopathy
- pregnancy
- obstruction distal to stone (ESWL can be used after stent or nephrostomy inserted)

Complications
- bacteriuria
- bacteremia
- post-procedure hematuria
- ureteric obstruction (by stone fragments)
- peri-nephric hematoma

A Comparison of Treatment Modalities for Renal Calculi Between 100 and 300 mm²: Are Shockwave Lithotripsy, Ureteroscopy, and Percutaneous Nephrolithotomy Equivalent?
J Endourol 2011;25:481-485

Purpose: To describe the outcomes of a series of patients who underwent shockwave lithotripsy (SWL), ureteroscopy (URS) or percutaneous nephrolithotomy (PCNL).

Methods: Patients treated for intermediate-sized upper tract calculi (100-300 mm²) at a single tertiary centre were included. Demographic and clinical data were collected from a prospectively maintained database.

Results: Of 137 patients, 38.7%, 29.9%, and 31.4% were treated with SWL, URS, and PCNL, respectively. Stone-free rate (95.3%) and single treatment success rate (95.3%) were highest for PCNL compared to SWL and URS ($p<0.001$). When allowing for up to two SWL treatments, success rates became equivalent for the three treatment groups ($p=0.66$). Auxiliary treatments were more frequent after SWL compared to URS and PCNL. Clavien grade complications did not differ between the three groups.

Conclusion: Up to two SWL treatments have equivalent success rate as compared to URS and PCNL. Hence, multiple SWL treatments may be a reasonable therapeutic option for patients who prefer SWL or who are not good candidates for alternative therapies.

Common Medications

Table 27. Erectile Dysfunction Medications

Drug	Class	Mechanism	Adverse Effects
sildenafil tadalafil vardenafil (PDE5s for use when some erection present)	Phosphodiesterase 5 inhibitor	Selective inhibition of PDE5 (enzyme which degrades cGMP) Leads to sinusoidal smooth muscle relaxation, increased blood flow and erection	Severe hypotension (very rare) Flushing, headaches, dyspepsia Contraindicated if Hx of priapism, or in conditions predisposing to priapism (leukemia, myelofibrosis, polycythemia, sickle cell disease) Contraindicated with nitrates
alprostadil (MUSE®), PGE_1 + phentolamine + papaverine mixture	Prostaglandin E_1	Activation of cAMP, relaxing sinusoidal smooth muscle Local release (urethral suppository)	Penile pain Presyncope
alprostadil, papaverine (intracavernosal injection) triple therapy also used: papaverine, phentolamine, PGE_1	See above	See above	Thickening of tunica albuginea at site of repeated injections (Peyronie's plaque) Painful erection Hematoma Contraindicated if Hx of priapism, or in high risk of priapism

Table 28. Benign Prostatic Hyperplasia Medications

Drug	Class	Mechanism	Adverse Effects
terazosin doxazosin	α_1 blockers	α-adrenergic antagonists reduce stromal smooth muscle tone Reduce dynamic component of bladder outlet obstruction	Presyncope Leg edema Retrograde ejaculation Headache Asthenia Nasal congestion
tamsulosin alfuzosin silodosin	α_{1A} selective		
finasteride dutasteride	5-α reductase inhibitor	Blocks conversion of testosterone to DHT Reduces static component of bladder outlet obstruction Reduces prostatic volume	Sexual dysfunction PSA decreases

Table 29. Prostatic Carcinoma Medications (N>0, M>0)

Drug	Class	Mechanism	Adverse Effects
leuprolide, goserelin *"androgen deprivation therapy"*	GnRH agonist	Initially stimulates LH, increasing testosterone and causing "flare" (initially increases bone pain) Later causes low testosterone	Hot flashes Headache Decreased libido
*cyproterone acetate	Steroidal antiandrogen	Competes with DHT for intracellular receptors: 1. Prevent flare produced by GnRH agonist 2. Use for complete androgen blockade 3. May preserve potency	
flutamide, bicalutamide	Non-steroidal antiandrogen	As above	Hepatotoxic: AST/ALT monitoring
abiraterone	Non-steroidal antiandrogen	Irreversible CYP17 inhibition, blocking synthesis of androgens in tumour, testis, and adrenal glands	Adrenal insufficiency (concurrent treatment with steroids often required) Hypertriglyceridemia Peripheral edema
enzalutamide	Non-steroidal antiandrogen	Androgen receptor signaling inhibitor (full antagonist)	Peripheral edema Fatigue and weakness Hot flashes

*Very rarely used

Table 30. Continence Agents and Overactive Bladder Medications

Drug	Class	Mechanism	Indication	Adverse Effects
oxybutynin	Antispasmotic	Inhibits action of ACh on smooth muscle Decreases frequency of uninhibited detrusor contraction Diminishes initial urge to void	Overactive bladder Urge incontinence + urgency + frequency	Dry mouth Blurred vision Constipation Supraventricular tachycardia
oxybutynin, tolterodine, trospium, solifenacin, darifenacin, fesoterodine	Anticholinergic	Muscarinic receptor antagonist Selective for bladder Increases bladder volume Decreases detrusor pressure	Overactive bladder Urge incontinence + urgency + frequency	As above
mirabegron	β3 agonist	Beta sympathetic receptor blocker in the bladder; relaxes bladder during storage phase	Overactive bladder Urge incontinence + urgency + frequency	Blood pressure should be monitored
imipramine	Tricyclic antidepressant	Sympathomimetic effects: urinary sphincter contraction Anticholinergic effects: detrusor relaxation	Stress and urge incontinence	As above Weight gain Orthostatic hypotension Prolonged PR interval
Botulinum toxin A bladder injections	Neurotoxin	Prevents the release of neurotransmitters	Refractory OAB incontinence both neurogenic and non-neurogenic	Urinary retention, UTI

Note: All anti-cholinergics are equally effective and long-acting formulations are better tolerated. Newer muscarinic M3 receptor specific agents (solifenacin, darifenacin) are equally efficacious as older drugs, however, RCTs based on head-to-head comparison to long acting formulations are lacking.

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